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A SYSTEM OF MEDICINE

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SYSTEM OF MEDICINE

BY MANY WRITERS

EDITED BY

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VOLUME I

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DEDICATION TO THE FIRST EDITION

TO

SIR J. RUSSELL REYNOLDS, BART., M.D., F.R.S.

PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS

THIS WORK IS DEDICATED

IN MEMORY OF THIRTY YEARS OF FRIENDSHIP

BY THE EDITOR

PREFACE TO THE PRESENT EDITION

The life of a system or text-book of medicine is comparatively short; and though the present work cannot be said to be out of date, it is desirable that a new edition should appear before the first has ceased to represent accurately the present position of medical knowledge. It is intended, therefore, to revise and bring out one volume a year, each new volume corresponding to one of the first edition. In this way the original edition will be gradually superseded by the new.

Volume II., which will, it is hoped, appear towards the end of 1906, is to be divided into two parts. The first will contain the important article on the General Pathology of Infection and Immunity, originally contributed by the late Professor Kanthack, and now revised and in parts rewritten by Professor Ritchie of Oxford; in it the chronic infections, the specific fevers, except those included under Tropical Medicine, the intoxications, and the other contents of the original Volume II. will also be dealt with. The other part will be entirely devoted to Tropical Diseases. In the arrangement of this portion of the work the Editors gratefully acknowledge the advice and help of Sir Patrick Manson.

The new edition is more than a mere revision. In most instances considerable additions to existing articles have been necessary; a number of the articles have been entirely rewritten, and several fresh subjects have been introduced. The first article in this volume—on the History of Medicine—is a new contribution by Professor Clifford Allbutt and Dr. Payne. The article on Medical Statistics has been entirely rewritten by Dr. Tatham, and is on somewhat different lines from that originally contributed by

Dr. J. S. Billings. The late Mr. Haviland's essay on the Medical Geography of Great Britain is succeeded by Dr. Clemow's more general article on Medical Geography. Sir Hermann and Dr. Parkes Weber's article on Old Age forms a natural complement to the article on the Hygiene of Youth. The arrangement of the article on Dietetics has been somewhat altered, and Dr. R. Hutchison has contributed the section on the physiological principles of this important subject. New articles on Exercise in the treatment of disease and on X-rays have become necessary, while it has appeared convenient to include among the Prolegomena an account of the Clinical Examination of the Blood and its Significance; this article really takes the place of that which previously appeared in Volume V. The article on Aerotherapeutics will be transferred to Volume IV. The important article on the General Pathology of New Growths has been entirely rewritten by Dr. F. W. Andrewes; that on Fever retains the historical retrospect given by Sir John Burdon-Sanderson, but now also contains sections on "Physiological Considerations" by Dr. Pembrey, and on "Clinical Considerations and Treatment" by Dr. Hale White.

Besides the Prolegomena, Volume I. contains some of the Acute Infections—but Cholera and Plague, which formerly appeared here, have been transferred to the Tropical Medicine section.

In recording some of the more prominent changes in the arrangement and treatment of the subject-matter, the Editors cannot but dwell on the memory of those colleagues whose help was given to the first edition, but whose voices are now still—Professor Sir G. M. Humphry, Professor Kanthack, Professor Leech, Sir R. Thorne Thorne. Their contributions have been revised by Professor Woodhead, Dr. Andrewes, Sir Lauder Brunton, and Dr. Hamer.

T. C. A.
H. D. R.

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DIVISION I

PROLEGOMENA

THE HISTORY OF MEDICINE

By Professor T. Clifford Allbutt, M.D., F.R.S., and J. F. Payne, M.D., F.R.C.P.

The medicine of Egypt and the East, extensive and intimate as it was, in so far as it was not Greek did not contain even the rudiments of science. To it Western medicine owes virtually nothing and, in this article at any rate, it may be disregarded.

Of Greek medicine[1] before the sixth century B.C. we should know little, almost nothing, were it not for the *Iliad* and the *Odyssey*. In the early centuries of Ægean civilisation medicine probably consisted of the following elements:—(*a*) fetish medicine; (*b*) demon medicine, which may have reached Eastern Europe from the Accadians; (*c*) theurgic medicine, or "temple medicine," which came to the Greeks from Egypt; and (*d*) a not inconsiderable knowledge of rough surgery, learned for the most part in the battlefield, and owing little or nothing to a study of anatomy. This fourfold system was rolled back, though not vanquished, by the scientific medicine of the schools of Hippocrates and of Alexandria. It is often supposed that scientific medicine sprang full-grown from the head of Hippocrates, for whom the way was prepared by the Ionic schools of philosophy, and especially by Heracleitus. However, the names of a large number of physicians before Hippocrates are given in the Aristotelian MS. of Menon. The disciples of Pythagoras are said to have dissected animals. His chief medical disciple was Alcmæon of Crotona, the Father of Greek Medicine. The works of Alcmæon are lost, but he exercised great influence upon Empedocles, Democritus, and Anaxagoras. Alcmæon practised dissection, and knew, for example, the Eustachian tubes and optic nerves. He believed the *anima* pervaded the body from the brain, and that sleep was due to a retreat of the blood from the finer to the larger vascular channels. The doctrine of the four elements—fire, water, earth, and air—which, when woven with that of the four humours—blood, phlegm, yellow and black bile—constituted the elaborate dogmatic system of later times, was formulated by Empedocles, with whom originated also the conception of the develop-

[1] I desire to acknowledge the courtesy of the Syndics of the Cambridge University Press who have permitted me to incorporate in this article the chapter on Greek Medicine lately written by me for their *Companion to Greek Studies* (1905).

ment of plants and animals, and of the survival of the fittest. Democritus is well known as the father of "materialism" (mechanical atomism).

Theurgic medicine knew many gods, and heroes such as Chiron, Asclepius, Podaleirius, and Machaon; yet it rose far higher than the fetish medicine of the Etrusco-Romans: indeed Apollo (in his medical attributes), Eilithyia, and Hygieia soon paled before the worship of Asclepius (Æsculapius), which seems to have originated in Thessaly, and not to have reached Athens till about B.C. 420. In Homer, Asclepius was a mortal chieftain, who seems to have had the root of science in him. Like Achilles he was a disciple of Chiron; and in his turn he taught medicine to Podaleirius and Machaon, chieftains of his own rank and kind. We may note that for the pestilence Calchas had no concern with medical remedies.

The apotheosis of Asclepius came later, and many temples were raised to him. We have record of about one hundred; those best known to us by their surviving relics were in Cos, Pergamum, and Epidaurus. Recent excavations in Cos have brought to light remains of an Asclepian temple with cells, the base of a statue, and the foundations of a well-house. If Tricca was the most ancient of the medical temples, Epidaurus was the largest, and the mother of many such health-resorts in Greek lands. These Asclepieia, whither, as to hospitals or spas, the sick were gathered together, were situated in places of fine air, pure water, and exhilarating scenery. In or near some of them were medicinal springs. There, beside religious rites, other physical and moral influences—such as the drama, games, social amusements, diet and training, and, perhaps, a few drugs—were brought to bear upon the sick in mind or body, as they are to-day at Homburg or Aix-les-Bains. At such resorts the effects of "Airs, Waters, and Places," and of regimen, as well as those of mental exaltation, diversion, or repose, were keenly observed by the positive Greek mind, and the results of these more natural methods quickly distinguished from those of priestly ritual. Thus medicine found its place as a branch of natural knowledge, a place which, after Galen, the last of the great Greek physicians, it lost again till the coming of Vesalius and Harvey.

At many of these resorts were medical schools, of which those of Ionian tradition, such as Cos and Cnidus, are best known to us; but the schools of Magna Græcia, Sicily, Cyrene, and Rhodes were more ancient. The school of Cnidus is said to have been of a dialectical and speculative bent; that of Cos laid stress rather on careful bedside observation, and on the study of atmospheric, telluric, and other external conditions; but our knowledge of Cnidus is mainly as painted by its opponents of Cos. The doctrines of the Greek physician were often erroneous in conception, but not often unscientific. His recognition of disease as a perversion of normal function, his vigilant reserve, his subordination of his art to the indications of nature, and his reliance on the *vis medicatrix naturæ* were in accordance with the best practice of modern times. The medicine of Plato (Timæus), though far from Hippocratic, was not quackery or

superstition. Aristotle, himself a physician who held a public medical office, and the son of a great physician of the seed of Asclepius and Machaon, owed much to Diocles of Carystus, and was destined to hold a perennial ascendancy over medicine almost to our own day. The sane and natural method of Hippocrates prevailed into the Alexandrian period, when it began to give way to a medicine of formulas and logical categories. On the other hand, Hippocratic medicine knew little of anatomy, the study of which was pursued in Alexandria with brilliant success. Physiology was established on an experimental basis by Galen (d. A.D. 200), but on his death fell into oblivion till founded again by Harvey in the seventeenth century.

That, as is generally stated, rational medicine was an offshoot of theurgic (temple) medicine is not clear; the modern visitor to Epidaurus may readily observe that the temple ritual was but a part, and by no means an overwhelming part, of the splendid apparatus built up by the clerical and lay managers of these health resorts. Indeed we have no definite evidence of the existence of a priesthood as a separate class; though there are some occasional indications in Greek literature that priest and physician acted together in some jealousy or rivalry. In early times the temples may have gone to the resorts of the sick; for in Homer no sick Greek or Trojan was carried off to a temple. It would seem that the temple methods were engrafted upon an ancient stem of secular medicine, Ionian or mainland, an alliance not inconvenient in a people so little superstitious or priestridden as the Greeks. Celsus gives honour to Hippocrates for the separation of medicine from philosophy, but on the connexion of medicine with religion he is silent. Even Herodotus avoids the supernatural origin of disease.

Of the part taken by priests in the cure of disease we know little precisely, but much may be supposed. By pomp, splendour, and ancient enchantments the senses were captured, and the springs of nervous energy unsealed; sorceries and impostures, which are apt to find their way into all great rituals, entered more or less into their system. And of such inspirations and suggestions the physicians may have availed themselves, directly or indirectly; it is alleged that mesmerism was a potent means in the hands of the priesthood. That patients were subjected to hypnotic suggestion we know with some fulness. In the age of Hippocrates it is probable that even the most sceptical inquirers harboured some belief in the supernatural origin of dreams; it is certain that dreams took a considerable part in the treatment of the sick, and that their value as means of "suggestion" was recognised down to the time of Galen. "Incubation," or "temple-sleep," was practised in the Greek temples, as in the Egyptian, under the hands of the priests. In the fatal illness of Alexander his generals had resource to it on his behalf. Incubation was by no means peculiar to the temples of Asclepius; it was practised at many other shrines; as of Apollo, Aphrodite, and Hera. The suppliants in crowds—the sexes were not segregated—their imaginations previously exalted by imposing rites, lay for sleep in the sanctuary by

night. If, as we hear, some were sleepless, the priests took care, no doubt, that they should see visions and hear prophecies nevertheless. Opium, hemlock, and some other sedative drugs were known in ancient times. In the visions the tame snakes kept in the temples played some part, as we infer from the *Plutus* of Aristophanes, from some of the inscriptions at Epidaurus, and from other testimony. Like the Delphic priestess, the priest of Asclepius also may have kept himself informed of the private concerns of the suppliants, at any rate of the more eminent of them; and we ourselves are in no position to denounce this blend of superstition, of the supernatural, and of natural and worldly wisdom, as mere quackery. Indeed, the Apolline religion may be regarded as an Ionian revolt from nature cults, gloomy, obscure, and corybantic, which then, as in other times and places, enslaved the thought and debased the passions of man. We may dwell rather on the therapeutical results obtained indirectly by the preparation for the vigils; this seems to have consisted in baths, fasting, purgation, anointings, and even bleeding: measures which had their vulgar advantages. On a larger scale, and more persistent method, these trainings, dietetics, mineral and sea bathing, and the like, fell in with the work of the physicians, and with the Greek cult of the body.

In the Asclepieia, as in S. Antonio at Padua and many other modern temples, certain important votive offerings were made, beside the precious metals. Some were pictorial or glyptic representations of diseased parts; or, especially in case of internal maladies, written records. It has been supposed, though on very slender grounds, that the clinical knowledge of the physicians was founded on these records, and so handed down in the medical schools. The Coan Prenotions and the first book of Prorrhetic in the Hippocratic collection are said to have been compiled from such sources, and even some of the Aphorisms also; though it is probable that the earlier aphorisms, with the aphorismic style, came from Egypt. Votive tablets, to have had this value, must have been dictated rather by the physician than by the patient; yet in the votive tablet the practice of taking clinical notes may have had its origin.

That Hippocrates—by which name we are wont to designate the most eminent of about eight Greek physicians who bore it—was of the Asclepiadæ, certainly does not prove that he was of the stock of Asclepius, a kinship which he never claimed; nor even that he was of a priestly caste: by the time of which we are speaking, at any rate, the Asclepiadæ had become what, in our own day, we call a college or guild. In early times Greek medicine seems to have been the inheritance of certain families not necessarily of sacerdotal tradition, and the brotherhood of blood gave way to the brotherhood of a corporation. In the *Iliad* we find that with the Greeks before Troy there were many of the craft, that they were held in the highest esteem, and that some of them, at any rate, were illustrious, even kingly persons. Idomeneus proclaims, Ἰητρὸς γὰρ ἀνὴρ πολλῶν ἀντάξιος ἄλλων. The field anatomy of Homer is by no means contemptible; he directs no strokes at random, and the heroes knew when a stroke was mortal or not. Nor was medical

practice all surgery. Opium, as I have said, was known from remote antiquity; Hesiod speaks of mallow and asphodel as medicinal; in the *Odyssey* Eumæus speaks of an *ἰητὴρ κακῶν*, in a context which suggests that even then physicians travelled from place to place, offering welcome service; and Nestor's wife Agamede "knew all drugs."

It is said that physicians were introduced into the Spartan army by Lycurgus, where they had a special camp. There are chapters in the Hippocratic collection on the surgery of war. Epaminondas had physicians with his forces at Mantinea; and Xenophon speaks, more than once, of physicians in attendance upon an army—there were eight at least with the Ten Thousand.

Of the constitution of the medical guilds we have some precious evidence in the well-known Oath (known as "of Hippocrates"); from it we learn that novices were solemnly initiated, and adjured to walk in the steps of masters who held up before their eyes a noble example of honour, integrity, obedience to the laws, secrecy, and loyalty to the interests of the patients under their care. We can scarcely doubt that this oath, which is older than the time of Hippocrates, owes its weight, austerity, and dignity to an ancient and honourable tradition of independence and responsibility.

Physicians of the school of Croton seem to have been regarded as the leaders of the profession in Hellas; and, a hundred years before Hippocrates, one of them, the celebrated Democedes, practised in Ægina, in Athens, and in Samos. Hippocrates (born B.C. 460?) was of Cos—the Mecca of medicine. Cos is an island near Rhodes, on the south-west coast of Asia Minor, and still bears the same name. The Coan School was flourishing in the sixth century. In the name of Hippocrates stands a large body of scriptures; some, such as the *De aere, locis, et aquis*, bear the stamp not only of a great and individual mind, but also of a mind positively scientific in bent and habit; in this work indeed may be found the germs of the kind of science in history which in our own time has been developed by such authors as Buckle and Taine; others are class-books and more or less rude collections of notes and aphorisms, in many instances significant of a true growth of natural knowledge such as we attribute to Ionia; others again, if we may judge by their doctrines, of Cnidian rather than Coan origin. All the books seem to be earlier than Aristotle, and in many treatises an older body of doctrine is assumed, and even quoted. Of some sixty works under the master's name, perhaps not six are from his hand; indeed, there is little better evidence to connect even these with the great Hippocrates than the internal evidence that they sprang from the mind of an individual genius, and the presumption that the doctrines of a teacher so venerated as Hippocrates would surely be preserved, either by his own hand or by the care of his disciples. Yet in view of the contents of the Menonian notes of Aristotle, in which certain highly speculative opinions on the *πνεῦμα* are attributed to Hippocrates, more caution than ever is necessary in relying upon the personal authenticity of particular works in the collection. It is probable, however, that these

speculations are to be attributed to Diocles of Carystus, a physician so distinguished as to be known as "alter Hippocrates," who flourished a little later. On the other hand, to speak of other works issued under the name of the master, of any of them indeed, as "forgeries," in the common sense of the word, is to ignore the history of all the ancient and medieval schools. Many were documents of the School, and current under the name of the leader of the School; others, not properly of the canon, or indeed of the same school of thought, were gathered into the collection more or less incidentally. Their various origin is proved by many inconsistencies of anatomical and other detail, as well as of style and doctrines.

Of the private practice of the Greek physicians we know little. It seems certain that some of them were attached, as teachers, to the schools. We know that eminent physicians were sent for by this tyrant or that, as Democedes by Polycrates, and detained about his person for large reward, and for long periods of time. It seems probable that Thales, who lived at the time of the Milesian factory in Egypt, studied in that country; and, as Hippocrates, like other philosophers, is known to have travelled widely, it may be assumed that he visited Egypt likewise. Eminent physicians on their travels were largely consulted on the way, and probably, after the manner of the Sophists, delivered lectures; thus perhaps may have arisen the class of "peripatetic physicians," if such a class there was. Some historians interpret the peripatetic as the practising physician, as contrasted with the physician of the closet; but Greek medicine does not smell of the lamp. In this sense it is not without interest to recall the Oriental custom of laying out the sick by the highways to solicit the advice of the passers-by. Other physicians were settled, for long periods at any rate, in particular places, and some of them received salaries from public funds. Democedes held an office of this kind, such as we call Medical Officer of Health, in Ægina, and afterwards in Athens. In ancient Greece any one might practise privately, but for State service certificates and guarantees were required; thus apprenticeships and schools arose, and probably there was a register. Midwives and "wise women" abounded, but no woman could be recognised as a physician. The position of official physicians is uncertain; in addition to Public Medicine, and provision against epidemics, they may have given instruction in dietetics and training. It seems clear, however, that the public physicians took also private practice for fees. The "Oath of Hippocrates," ancient as it probably is, seems to contemplate private practice almost exclusively; and we may note that in it the title of Asclepiad does not occur. The public physicians were men of substance and dignity; and, wild as are some of the modern computations of their gains by salary and fee, in many instances their earnings seem indeed to have been very large. It may be that the salaried physicians had to attend the poor gratuitously; it is certain that Greek physicians of this period gave freely to the poor and to the stranger not only of their skill but also of their substance.

In the gymnasia training and dietetics were developed, and in them

especially arose that surgery of fractures and luxations which in the time of Hippocrates had attained an eminence admirable even from a modern standpoint. It would seem, moreover, that cases of chronic disease were often submitted to the hygienic regimen of the gymnasium.

The physicians kept offices or shops supplied with a large variety of surgical and other instruments, dressings for wounds, and drugs, of which last there was a customary but not an official list. In these offices, and also by druggists (*φαρμακοπῶλοι* and *ῥιζοτόμοι*), medicines were dispensed by the single dose or in larger quantities. Moreover, to these medical homes patients were often removed for closer observation or for special treatment. There was a public *Ἰατρεῖον*, or "Surgery," also in every large city, maintained out of taxes or rates. Slaves were employed as assistants and dispensers. The physicians had also cases fitted with medical and surgical appliances, which they carried with them on their travels. Lofty in ethical standard and pure of all charlatanry as was the school of Hippocrates, too often, in later centuries at any rate, medical practice thus became a trade; and these offices, like barbers' shops in more recent times, became places of call, not always to the honour of the profession. Indeed, we are told that in ancient Greece, as in medieval Europe, certain elegant and well-dressed physicians were wont to rely rather on personal attractions than on scientific acquirements; and that others descended even to the level of quacksalvers and criers of medical wares in the markets. In Egypt specialism in medicine had been carried to the absurdest extremes. In Greece this unscientific dismemberment of the profession was not practised to any mischievous excess; but we know from the Oath of Hippocrates that cutters for stone were specialists, as also were oculists and dentists (gold-stopping of teeth is a very ancient practice). Surgery, in its graver operations, was in early times a very perilous calling; and probably in ancient Greece, as certainly in medieval times, local practitioners were wont to entrust the graver operations to peripatetic craftsmen, who took care to disappear before the issue of their work could be known.

We have seen, then, that medicine, as a natural science and rational practice, always enjoyed in Greece a peculiar independence of the hierophant and the philosopher. The school of Hippocrates was a school of watchful observation of nature, though not of experimental verification; a school devoted to description of diseases—chiefly of the acuter kinds, and of these chiefly the fevers—as orderly sequences of symptoms classifiable under certain types, and also to the study of constitutional proclivities, but not of accurate details or subtler distinctions which at that time were scarcely possible. It was a school of careful observation of external but not of inward causes, nor of the local seats of disease, for of course pathology was rudimentary. The pride and the proof of Greek medicine was prognosis, which was aided or perverted by the pythagorean doctrine of "critical days." In therapeutics it was a school of vigilant waiting upon nature, and of the use of physical means such as diet, waters, fresh air, and gymnastics; not of violent interference by bleedings, by drugs,

or by empirical specifics. Its honourable motto was—The physician the minister of nature. In this direct and natural study of facts surgery made remarkable progress. By his surgical training it was that Hippocrates was led to announce clearly and categorically the first principles of inductive research and practice; namely, phenomena first, then judgment, then general propositions, then practical knowledge and craft. One principle only, but that a great one, was wanting to him, namely, experimental verification, a principle not definitely apprehended by Aristotle, nor, so far as we know, by any ancient physician except Galen.

Little as the fifth century knew of inward anatomy, as compared with Alexandria about two centuries later, yet the marvellous eye and touch of the Greek physician had made an anatomy of palpable parts—a clinical anatomy—sufficient to establish a Medicine of some parts of the body of which our own generation would not be ashamed. The patient was stripped and examined from head to foot—his build, and the conditions of chest and abdomen, of the skin and mucous membranes, were carefully noted, the temperature of parts were estimated by the hand, and all excretions scrutinised.

In respect of fractures and luxations of the forearm, M. Pétrequin pronounces Hippocrates more complete than Boyer; in respect of congenital luxations richer than Dupuytren. Malgaigne again admires his comparison of the effects of unreduced luxations on the bones, muscles, and functions of the limb in adults, in young children, and before birth, as a wonderful piece of clinics. In Littré's judgment the work of Hippocrates on the joints is a work for all time. On wounds, which in warlike and unruly ages have constituted the principal branch of surgery, Littré says that the Hippocratic books must be studied with deep attention. The wound surgeons of the Hippocratic school were indeed far better instructed than those of the medieval and renaissance periods. If poultices were used they were to be applied near but not upon the wound; the water for washing the wounds, unless very pure, was to be filtered and boiled, their linen dressings were of new material, and the hands and nails of the operator were cleansed. Of the access of air to the wound the Greeks were very jealous, a jealousy which led to much abuse of the suture in later times. In fresh wounds they anticipated healing by first intention, but in less recent and in contused wounds suppuration. To foul wounds certain balsams were applied. Wound-fever was known to the school, and the different significance of fever in the first week and in later weeks was pointed out. Puerperal fever was interpreted as a wound-fever, and its occasional origin in retention of putrid uterine contents was recognised. In wounds of the head Hippocrates warns against careless interference with the temporal regions, lest convulsions and palsy occur on the opposite side of the body; for the trepan was then in vogue, as it had been from the darkest backward of time. In spinal injury he notes that incontinence of urine and fæces is of fatal augury. Empyema and pyelitis were

operated upon. From amputation of the larger limbs he flinched, as did most if not all responsible surgeons down to Paré; for inner anatomy was ill-known, and ligature of arteries, even in wounds, made slow way; indeed, before Celsus this method seems to have been unknown. Of obstetrical practice I must be content to say that it had reached a high standard; when surgery flourishes obstetrics flourish.

After the Hippocratic period, under the Macedonian supremacy, medicine was high in court favour, and on the whole was progressive, as was natural science also. On his expedition to the East, Alexander carried with him naturalists as well as historians and literary men. Theophrastus advanced the knowledge of pharmaceutical botany as well as the anatomy and physiology of plants. He investigated physics also, as the phenomena of light, and has left interesting descriptions of minerals. Of this period were Diocles (p. 6), Chrysippus of Cnidus, and Praxagoras of Cos (the tutor of Herophilus), who proposed abdominal section for ileus, but is better known as one of the first to explain the arterial system and its pulses as the function of the "pneuma." By him was laid the foundation of the scholastic pulse-lore, which became as pedantic and tiresome as the rest of medieval dialectics.

The schools which claimed to stand in the direct following of the Hippocratic tradition became known as the Dogmatists. Their danger was the pedantry of elaborated doctrine; their merit the respect for the ancillary sciences and for rational processes of clinical investigation, as opposed to the formulas of the Methodists, and the hand-to-mouth practice of the Empirics.

It was, however, in Alexandria that Medicine rose again, with the marvellous Greek fecundity, under the Ptolemies, especially under Ptolemy Soter (B.C. 323-285). To Egyptian tradition it owed nothing, unless it were an aversion from drawing of blood (the life); the centre of gravity of Hellenic policy had swung from Athens to Alexandria, and in the extraordinary progress of anatomy the impetus of Aristotle was continued, and a broad foundation laid for Galen. The two chief figures among the Alexandrian physicians were Herophilus and Erasistratus, under whom not only descriptive anatomy advanced, but also the conception of local seats of disease. Their works are lost, but we obtain some little knowledge of them from Galen and later authors. Surgery and gynæcology, as we should expect in an anatomical school, made more progress than inner medicine. At this time also many of the chief schools of medicine seem to have been in Asia Minor, as in Pergamum, Ephesus, Tralles, Miletus; and before this period Greek physicians had penetrated to the Persian court, and still farther into the East, where they were held in honour, and where some of their doctrine survived.

But the great epoch of Alexandria was not long dominant. Although the school did the incomparable service of collecting and sifting the works of the Hippocratic period, medicine began to forget this broad and sane example, and broke up into narrow sects, dependent upon scholastic philosophies; and in practice polypharmacy and the lower forms

of empiricism prevailed. The sceptical school of Pyrrho and Carneades, the influence of which on medicine was pernicious, fortunately never got any great hold upon it. It was from stoicism rather, which subordinated science to ethical and practical ends, that Serapion (end of third century) and the sect known as Empirics arose, a school which professed to concern itself only with the detail of symptoms and remedies, to the neglect of anatomy and physiology, and of reasoning on the nature and origin of disease. To this sect medicine owed the grievous antidotes of mithridatics and theriacs, and other manifold and grotesque receipts, which were greedily sought as defences against the arts of the poisoner.[1]

And now to Rome, the builder of the body of Western Europe, the Hellenic spirit was carried, *et artes Intulit agresto Latio*: there in the second century A.D., after it had been long defied by Cato and his followers, Greek medicine prevailed, as Italian medicine penetrated into England in the reign of Henry VIII. Roman or Etruscan medicine, before the Hellenic influence, was but a medicine of oracles, charms, and nostrums, on which we need not dwell. Asclepiades (b. *circ.* B.C. 124), a Bithynian, the friend of Cicero and Crassus, and a man of fashion but of some genius, was the first eminent physician of the Greek school in Rome. By Tiberius the office of Court Physician was established. Asclepiades, his pupil Themison, and Thessalus of Tralles, followers of the atomic hypothesis of Democritus and Epicurus, founded in medicine the sect of Methodists, whose principle was that health and disease depended upon what we now call tonicity, a right balance of the *strictum* and *laxum* about the "pores" of the body. Diseases for them depended upon the undue predominance of the one condition or the other, though like other system-builders the Methodists had also to suppose a "mixed condition." The study of anatomy, and of the causes or seats of diseases, even diagnosis itself, thus became superfluous. Of this school nominally, though far superior to it, was that great physician, Soranus of Ephesus, a contemporary of Galen, but a little older than he, of whose works unhappily only the gynæcological portion survives; though the treatises of Cælius Aurelianus, who lived about three centuries later, on "Acute Diseases" and on "Chronic Diseases" are but a version of Soranus. The doctrine of the Methodists, as interpreted by the Eclectics, survived until the sixteenth century, and was virtually resuscitated by the Brownists at the end of the eighteenth. The school which stood in the following of Hippocrates, though unfortunately rather on its speculative side—even to the fantasy of eleven humours!—was called the Dogmatic. Still, the Dogmatists protested that medicine must be based on a physiology, and "they are the fathers of modern medicine."

In the architectural works of Vitruvius it is interesting to note the regard for public health, and especially the recognition of the poisonous effects of lead in drinking water, and of working in lead.

[1] For an appreciation of the Dogmatic and Empirical schools see Celsus, *De Medicina*, Introductory chapter. For a rapid yet vivid glimpse of the medical history of classical times, I cannot too strongly recommend the perusal of this brief but admirable Introduction.

The fashion of encyclopædic collections of all knowledge—of "Summæ"—which formed a literary habit in the Middle Ages, may be said to have begun with Celsus. Celsus seems not to have been a practitioner of medicine, but he wrote a work on Medicine, which probably was a section of such a "Summa," other sections of which, as on Agriculture, War, and Rhetoric, are lost. To this admirable and precious book we owe the chief part of our knowledge of the history of medicine between Hippocrates and Galen. Celsus deals with all the diseases known in his day, and hands down to us much of the Alexandrian surgery, such as plastic operations, cutting for stone, amputation in gangrene, and cataract operations. By his literary style, Celsus did much to found medical latin. Another summist was Pliny the Elder, who wrote a well-known Natural History, which in respect of medicine concerned itself largely with pharmacy. For his services to botany he is to be ranked with Theophrastus.

From this time to that of the Antonines, medicine, both in West and East, was in vigorous growth and in civic honour. The school of the Pneumatists, the origin of which I have already indicated (p. 9), largely reinforced by Erasistratus, obtained considerable vogue under the leadership of Athenæus of Attalia or Tarsus (fl. first century A.D.), of whose writings some fragments remain. The Pneumatists did service in putting forward the dynamic aspects of life, and in hygiene of body and mind Athenæus was a master. This school was merged in the Eclectic, of which I have already spoken. In these schools Rufus of Ephesus, Aretæus the Cappadocian, and Archigenes of Apamea were eminent as leaders. Archigenes was perhaps the first to dwell upon the need of a pathological anatomy. It is somewhat remarkable that a physician so rich in experience and so sober in reason as Aretæus had little influence in the Middle Ages. He was probably contemporary with Rufus and Soranus, that is, about the end of the first century; and, as with Celsus, much that we admire in him he probably owed in substance to his predecessors, and put into excellent greek. Of his valuable contributions to Medicine little account can here be given; but allusion must be made to his description of the Syrian angina, which was probably diphtheria. Archigenes seems to have done great service in surgery, but he is known to us only in the extracts of Oribasius. Heliodorus lived in Trajan's time; he used torsion in arterial hæmorrhage, operated on stricture of the urethra and on hernia, and resected bones. Antyllus seems to have been a masterly surgeon who ligatured aneurysms, extracted (so says Razes) the lens in cataract, and improved the plastic operations which in the Middle Ages had so remarkable a success in South Italy. But as all this literature has vanished we depend for these details upon Oribasius. In their acceptance of the ancillary sciences, and in their recognition of a larger function of reason than the mere accumulation of detail which contented the Empirics, the Eclectics reformed medicine and prepared the way for Galen. In Galen, Greek medicine found at once its culmination and its eclipse. This extraordinary man, the founder of

physiology by the true way of the experimental method, a prodigy of learning, and only too copious and ingenious a philosopher, stood eminent on the abyss which in after-time swallowed up medicine and all natural science for more than a thousand years, until in the universities of North Italy the medicine of the West was born again under the spell of Vesalius and Harvey.

To give a just appreciation of Galen in a few lines is impossible, indeed an appreciation just and full has yet to be written; but from a few selected particulars some notion of his work may be gathered, and some illustration of the growth of medicine at the crucial time of the second century. Galen was born at Pergamum A.D. 131, and died A.D. 210. He was a man of fortune and high personal ascendancy. He travelled widely, and studied especially in Alexandria. He lamented the schism between theory and practice, and sought to bring them together by means of a thorough study of structure and function based upon observation and experiment. To this end he devoted himself personally to investigation of the nervous system, and with marvellous success. He arrived at some broad conception of the *sensorium commune*, and of its warning functions in respect of useful and harmful conditions; he showed that the meninges are insensible, that much of the brain may be ablated without paralysis until the central ganglia are reached, and yet that to invade the region of the fourth ventricle is perilous to life. Of the nervo-muscular mechanism of respiration he discovered the main features; for example, by proper sections he contrasted intercostal and diaphragmatic breathing, and demonstrated the effects on the respiration of opening the pleural cavity. He performed hemisection of the spinal cord, thus producing spinal hemiplegia, and he distinguished by precise experiments the sensory from the motor roots. He showed how lesion of the spinal cord may paralyse the bladder. He divided the pneumogastrics, and thus palsied the voice. He contrasted the purely motor nerves of the orbit with the mixed trifacial. In the hand he demonstrated the distribution of sensory nerves to the skin, of motor fibres to the muscles. He may fairly be said to have apprehended what we now recognise as nervo-muscular tonicity; and, furthermore, that variety of function depends not upon quality of nerve fibre, but upon that of end-organs. Among many clinical observations I will cite only his discrimination of paralysis agitans from other tremors, and of cerebral from gastric vertigo. Rigors for him meant pus; and the expectoration of false membranes, a dangerous inflammation of the air passages. As a physician Galen was a disciple of the school of Hippocrates (the "Dogmatists"), he relied upon the tendency of the body to recovery, and made careful use of exercises and dietetics. In pathological anatomy Galen did but little, yet of diagnosis he discerned the three aspects—the part affected, the causes, and the various grouping of symptoms. He held that there could be no disorder of function without a lesion of a part, far as the part might be from the morbid effect, as *e.g.* loss of voice from an injury to the thorax. He goes so far indeed as to suggest that

for cure it is important to know the nature of the local lesion. As to physiology, when he left the dissecting-room Galen spun it into philosophical cobwebs, and indulged himself in extravagant speculation; thus he elaborated the functions of the "pneuma," and the doctrine of the four elements and four humours, and of the diatheses, into a network in which medicine was entangled for some fourteen centuries; and, outdoing the great Stagyrite himself, carried final causes into every part and aspect of physiology—an ingenuity which made his doctrines especially available for the Church.

The power and splendour of Rome under the great Spanish Emperors, and the power and honour of medicine under Galen may be taken in this brief essay as a convenient period whence to contemplate their decline. Both for trade, arts, and war the centre of gravity of Europe shifted to Byzantium. As war was no longer for empire but for the defence of the Gate of the West, so medicine withdrew from the expansive animation of Archigenes, Heliodorus, Galen, and Antyllus, to the humbler office of conserving its traditions. Thenceforward, for some fourteen hundred years, medicine suffered little change of standards, of doctrines, or of methods, till in the later Middle Ages the machine was set in motion again by its surgical craftsmen, and in the seventeenth century by the quickening of the natural sciences. Academically speaking, medicine, from the death of Galen to the birth of Harvey, was kept alive by the vigorous schools of Italy, yet made little growth. And as the bulwark of Europe, the Rome of the East, was battered and despoiled, so was its freight of medicine broken up and trodden under foot. For many centuries thereafter, the history of medicine is a history not of growth but of salvage, a history of the salvage of fragmentary and corrupt records floated on rafts down the long streams of time.

The main streams on which dismembered parts of the body of medicine thus drifted down to us were three—the byzantine, the arabian, and the neo-latin or romano-greek;[1] but these streams were not like rivers separate and divergent, but rather like the currents of a sea pouring through several channels to sweep again into one tide. The byzantine channel joined the syrian and arabian, the hellenist the latin; the sources of Bagdad and Constantinople, Cordova and Montpellier, Salerno and Bologna, ultimately united in the flowing tide of Vesalius, Paré, and Harvey.

The complexity of the factors of human society is well illustrated in the far-reaching consequences of a religious heresy upon the fortunes of medicine. In the fifth century the Nestorians, driven into Asia, not only founded great schools of medicine, for example, at Edessa in Syria, and at Gondisapor in Persia, but by their missionaries hellenistic medicine was carried far and wide through the East, certainly into Mongolia and India, probably even into China. The neo-latin stream meanwhile shrank to the scantiest rills. If, with the spread of Christianity, the charity and pity

[1] It must be remembered that South Italy long remained a part of the Eastern Empire, and there in some fashion greek survived till the Middle Ages.

of hellenic times grew into a new relation to life, and received a new inspiration, so that refuges and hospitals increased and were multiplied, yet, on the other hand, in the Christian contempt of the body the admirable Greek hygienic systems—the baths, the gymnastics, and the dietetics—fell into neglect, and medicine was loaded, perverted, and obscured by neo-platonic mysticism, stereotyped receipts, oriental magic, and superstitions favoured by the Church. The great Romano-greek physicians who flourished between Celsus and Galen had no masterly successors; and the schools of the West, such as they were from the third to the twelfth century, lived on such dry bones as abstracts of Pliny and Theophrastus, and such flotsam of Hippocrates, Aristotle, Galen, Celsus, Cassius Felix, Cælius Aurelianus, Dioscorides, Scribonius Largus, Sextus Samonicus, Vindicianus, and Theodore Priscian, as in one guise or another drifted within the latin ken. Unfortunately the works of Celsus were not widely or continuously known in the Middle Ages.

Theodoric, the Ostrogothic master of the Western Empire (A.D. 454-526), made a serious attempt to restore the art of medicine. His minister, Cassiodorus, procured latin translations of portions of Hippocrates and Galen; and Isidore of Seville and Boethius did a like service. In the seventh century, indeed, public lectures on these authors were delivered at Ravenna; and latin versions of extracts from Oribasius, Alexander of Tralles, and Dioscorides, in uncials of the seventh to the tenth century, are or were to be found in such libraries as those of Chartres, St. Gall, Monte Cassino, Einsiedeln. West of the Adriatic and north of Calabria greek was virtually unknown; even so distinguished a scholar as Gregory of Tours (sixth century) knew but a few words of greek liturgy; but traditional glossaries survived, as in Isidore and Gariopontus, one of the earliest of the Salernitans known to us. The origin of these latin versions is almost beyond conjecture; they may have been made by greek physicians in Gaul, but I would suggest that some of them at any rate were made for Salerno by the Calabrians of the Eastern Empire. At a later date (fourteenth century) we know that Calabrians such as Nicolas of Reggio were translating Galen, and thus preserved for us certain tracts otherwise unknown. The problem is not one of mere curiosity, for corrupt or errant as these texts may be, and deformed as may be their latin, yet in not a few cases, as in Paul's plagiarisms of Oribasius, they represent older greek texts than any now extant.

In the Merovingian and Carolingian palaces schools were encouraged, and under their dukes we read of "archiaters" and public physicians, and of physicians devoting themselves to the suffering in the great pestilences of the fifth to the tenth centuries. In the cloisters, churches, and bishops' houses also were clerical schools; in them Charlemagne and Alcuin gave an enlightened favour to medicine, and thus the flax smouldered till the eleventh century, when it was fanned into flame by the breezes of the new science and philosophy which flowed into Western Europe from Cordova and other Arabian sources.

In the Eastern Empire the central stream of the period which in the

West was called the Dark Ages, though a stream of conservative tradition rather than of development, was one of richer volume. Encyclopædists rather than investigators, priests of medicine rather than its makers, were such chroniclers as Oribasius, Aetius, and even Alexander of Tralles. The compilers, Oribasius especially, have preserved for us, but unhappily only as embalmed fragments, some records of the medicine of the West after Galen, of the medicine of such masters as Heliodorus and Antyllus (p. 11). Byzantine medicine, primarily hellenistic, slowly taking on the features of many times and folk became medieval in character; though it would be truer still to say that by virtue of its immense and imposing organisations it impressed much of its own features upon the Middle Ages.

Of the compiling physicians of the conservative period between Galen and the first stirrings of medieval medicine in Salerno, Oribasius was the chief. In worldly position, as a man of family and fortune, and of professional and political distinction, he reminds us of Galen. As one of the last of the pagans he was closely attached in politics and friendship to the Emperor Julian, who promoted him to be Quæstor of Constantinople. Oribasius was born in Pergamum—the mother-city of many eminent physicians—about 325 A.D. In original gifts he is not to be compared with Galen, or with any of the greater physicians of more ancient times, yet gifts he had which for us have been no less useful. As a compiler he shows excellent judgment, and stands for many centuries almost alone in careful attribution—for the greater part at any rate—of his quotations to their respective authors. He had in large measure the gifts of an editor. At the desire of Julian himself Oribasius collected, under the title of "Synagogæ," an encyclopædia, in seventy books, of medicine, hygiene, therapeutics, and surgery. His extracts begin soon after Hippocrates, but as they are more various and extensive after Galen and near his own times, a period during which the loss of medical books has been ruinous, and the copies which have reached us late and corrupted, these collections are very precious to the historian. When manuscripts were cumbersome and very costly, it was the custom of authors of large works to issue synopses, *summulæ*, or *opera parva* which were portable and cost comparatively little; unfortunately the vogue of the abridgment involved the neglect, and too often the ultimate disappearance of the whole or part of the complete work. Two such synopses were issued by Oribasius, and of the complete collection more than half disappeared from the time of Paul of Ægina (seventh century), and with the lost sections we have to deplore much of medicine and surgery. In some measure, however, the gap is filled by the scantier and less trustworthy sixth chapter of the Tetrabiblia of Aetius, and by two books on diseases of women and children, discovered by Dietz, which were compiled from Diocles, Mnesitheus, Athenæus, Rufus, Soranus, Galen, Antyllus, Philumenus, etc. The great Arabian Razes did most to make the collection of Oribasius known in the Middle Ages; and to Bussemaker, Daremberg, and Molinier we owe an admirable modern edition; yet these editors themselves tell us that

the criticism of this great storehouse is not finished, especially in respect of botany, mechanics, mineralogy, and greco-roman archæology.

If in the period between Celsus and Galen the procession of physicians is known to us by little more than their names, yet in this little we recognise the shades of great men in medicine. Even in the period between Galen and Oribasius we have impressive fragments of such physicians as Antyllus. If to us little more than names, yet their names are great and memorable. *Ex pede Herculem.*

In the period between Oribasius and the school of Salerno, the period of the little Greek writers, we have names and fragments; but the names have for the most part but an antiquarian interest, and the fragments are only precious to us in so far as they are crumbs from the tables of their greater ancestors. For these men departed from tradition and convention only so far as to trick out their formulas and manœuvres with the magic of oriental and sacerdotal superstitions. Of these wraiths the only one of much personal distinction is Alexander of Tralles. Aetius and Paul of Ægina live for us only as adorned with other feathers than their own. To Alexander we will return presently. Aetius of Amida (a city of the upper Tigris), who flourished about the middle of the sixth century, put together a treatise on previous and contemporary medicine, based, as medicine mainly was when its active growth ceased, on the narrow rule of the Methodists and the unreasoning practice of the Empirics, and coloured by Christian mysticism and pagan superstition. His works did not exercise any considerable influence during the Middle Ages, as more than once they were lost or forgotten. To us the interest of his Tetrabiblia is that they compensate in some degree the loss of parts of the collection of Oribasius.

Fortune is capricious in her favours: Paul of Ægina flourished at the end of the seventh century, and dry copyist as he was, chanced to have a great and beneficent influence on medieval medicine. In those days, as in our own, surgery was the laboratory of clinical medicine, its scientific arm. Only by surgery was medicine in the Middle Ages kept forcibly bent to the facts. Now, in his sixth book, Paul handed on from a lost section of Oribasius the Celsian tradition of surgery, and was in his turn copied by the Arabian physician Albucasis, whose treatise from the twelfth to the fifteenth century had a great vogue in the West. In other parts of his work Paul helped himself freely to Alexander of Tralles, whom, however, he scarcely mentions by name. After Paul abstracts and manuals became more and more jejune; physicians lived on loans, knowing not whence their little knowledge came—on links of tradition and embalmed bits of learning, perverted, especially in the East, by sophistry and magic. The medicine of the sixth to the eleventh century has been described as a few dark and bad paths among ruins. But for a moment some brighter rays were shed on these paths, in the reign of Justinian, from Alexander of Tralles, near Ephesus. Like Galen and Oribasius, Alexander was a person of quality, the friend of an Emperor, and the brother of the architect of the superbest church in Christendom.

In reading the works of this natural and modest writer, who had travelled East and West, who had seen beyond the narrowness of the Empirics, and through the empty speculations of other schools, who had sense enough to return to the true paths of Hippocrates, Diocles, Archigenes, and Galen, and also was yet independent enough to follow them with discrimination, one is tempted to a petulant disappointment that he was not still greater; that he made no advance in anatomy or physiology, but was entangled in pneumatism and humoralism; that, as apparently no surgeon, he was not trained upon the positive side of medicine, and that he permitted himself to traffic even with amulets and incantations. It is more equitable, however, to remember that at the brightest period of the Byzantine age, when, for too brief an interval, the arts and humaner social institutions were in the ascendant, Alexander had not only the abilities and the knowledge but also the humanity which, exercised at such a time, made for a renewal of standards, intellectual and ethical, which were not altogether forgotten in the confusion and rapine which ensued, when Rome, under the exarchate of Ravènna, was harried by the Lombards, its domains became waste and pestiferous, and the City of the Seven Hills fell into the place of a second-rate town. Although, as will appear hereafter, the parent medical school of the Middle Ages owed but little to Arabs, Jews, Benedictines, or Charles the Great, nor much indeed to the first translators from the arabic, Constantine and Gerard, yet Salerno, as we see in Roger and Gariopontus, inherited much from Alexander. Constantine's "Viaticum," derived through Isaac the Jew, was founded upon Alexander's writings. Gerard's "Summa parva" was a version of the same. To the shortcomings of Alexander I have alluded: his strength lay in his distinction between external and internal causes; he regarded diagnosis as the rudder of practice, and examined the body as punctually as Hippocrates. In practice he was mild, reasonable, and cautious, and fixed attention on prevention and cure as the ends of medicine. In dietetics he was vigilant, and he made no little use of baths and mineral waters. When in Constantinople men were dying at the rates of five to ten thousand a day, he devoted himself nobly to the care of the sick.

While with the Neo-latins we have seen that medicine, choked in ignorance and confusion, almost ceased to exist, and that with the Greeks it survived rather in suspended animation than in growth, we have now to turn our eyes to the Crescent, and to admire one of the most remarkable phases of the history of culture, the phase of Saracenic civilisation whereby, in a circuitous but brilliant orbit, the potent influence of the medicine, the philosophy, and other learning of pagan and Christian Greeks swept round to the West, then divided from the East by a chasm of enmity far deeper than the breadth of the principalities of Western Asia, Egypt, Syria, and Andalusia. But the splendid era of the Caliphs of Bagdad, and of Spain, and in no small measure of Egypt, was as transitory in time as it was abiding in its results. The Arab culture was, it is true, a second-hand culture: but if the Saracens had not the

genius of creation they had in singular measure the genius of selection and of appreciation. If, moreover, they brought into Europe the oriental impostures of astrology and alchemy, with these baser alloys were accumulated and poured in upon Europe enormous treasures of true metal. The barbarous Roman, the barbarous Arab, and the barbarous Goth, if themselves uncreative, had at least this salvation, denied to the modern philistine, of wonder and admiration before the culture of their captives.

[Since this article was written M. Cavvadias, whose authority as a scholar and archæologist, and indeed as the director of excavation at Epidaurus, commands immediate attention, has published his opinion that in the Temples the sick sought relief not from human skill but from divine intervention; and that before the Roman period medicine had no place in these sanctuaries. In his opinion the dedicatory inscriptions, to judge from those which have been discovered, had no scientific value whatever.]

T. Clifford Allbutt.

Medicine in Modern Europe

By J. F. Payne, M.D., F.R.C.P.

The Dark Ages.—Without presuming to define precisely that historical period to which the name of the Dark Ages has been given or to justify the appellation, we may safely say that as regards medicine the period from the fifth to, say, the tenth century well deserves to be called "Dark" in Western Europe. The old Græco-Roman medicine declined and became forgotten, the schools were closed, libraries destroyed or neglected, the great traditions of surgery were lost, and almost all links with the learning of the past were broken. Moreover, as we have seen, medicine suffered not only from decay but from the introduction of a new and baleful influence—that of the Oriental magic, which, spreading from the East, involved the whole Roman Empire in a dense cloud of superstition. Magic itself and its origin are subjects too large to be touched upon here, but in medicine we know what it meant. It meant the introduction into the healing art of magical rites, of charms and incantations, or amulets; of all kinds of superstitions, borrowed, many of them, from the old beliefs of primitive peoples.

In few countries has the art of healing ever been free from superstition, but it was the especial glory of Greek classical medicine to have banished these things from the practice of the art. The later Greek physicians of the East, Aetius, Alexander, Paulus, yielded in some measure to this baneful influence, but in the West its triumph was more complete. It weighed upon European medicine as an incubus for several centuries. We must pass lightly over this dark chapter in the history of medicine, but observe that the later Latin medical literature exhibited this superstitious element in its grossest form. The work of Marcellus Empiricus, *De Medicamentis* (to take one example only), very popular for centuries, is a mere farrago of some precepts of the older medicine, mingled with Oriental superstition, Christian charms, folk-lore of Roman, and probably also of Celtic origin,

exhibiting altogether, perhaps, the lowest level to which medicine among educated people could sink.

The Church, while it condemned the Oriental magic, without doubting its power, as being of Satanic origin, maintained a superstitious atmosphere by its own system of miraculous healing. For the impious charms and magical rites of the heathen were substituted invocation of Saints, pilgrimages to sacred shrines, and the like. To put trust in these methods was held to be more pious as well as more efficacious than to have recourse to secular medicine. Miraculous cures happened every day, and in the organisation of their system of "faith-healing" the ecclesiastics of the sixth century went far beyond the practice of prayers, inunctions, and laying on of hands in which the early Christians put their faith. The ritual of miraculous cure, as practised in the south of France, might have been borrowed from that of the temples of Asclepius in Greece. Incubation in the sacred building, watching for the vision in the night of the Saint who was to heal the worshipper, directions for cure uttered by a sacred personage—all these details were revived (*vide* p. 3).

A more pleasing picture is afforded by the one branch of the ancient medicine which never entirely died out in the darkest ages—the knowledge of medicinal herbs. Among the late Latin medical writings we find herbals, based chiefly on fragments of Dioscorides and Pliny, and often illustrated with traditional figures of plants intended to show what was meant by the old names. These books were the manuals of the Benedictine monks, who, while cherishing some remains of the old medical lore, were never without a herb garden to provide their simple remedies, which were always at the service of the poor. The herbal medicine steadily held its ground, and was one of the foundations on which this low reconstruction of medical science was based.

In one corner of Europe grew up a medical literature, limited in scope and short in its duration, which yet formed a luminous episode in the prevailing gloom. The Anglo-Saxons, long before any other Western nation, attempted to construct a medical literature in their own tongue, compiled out of fragments of Greek medicine in Latin versions and some original knowledge of herbs, but mingled with Oriental and Christian superstition, simple and almost childish in form. These works have no great intrinsic value, but our countrymen have this merit, that, contemporary with Razes, before Avicenna, and earlier than the earliest known writers of the school of Salerno, they produced the first medical treatise compiled by any of the modern nations of Europe.

The School of Salerno.—In the general darkness one spot of light became visible, and grew till it illuminated, in some measure, the general face of medicine in Europe. In Salerno, a town on the coast of Southern Italy, a region where the Greek language, and possibly some Greek culture, still lingered, arose the first school of medicine in modern Europe, and the first European University. The origin of this school is, and perhaps will always remain, obscure. When the light of

history is first thrown upon it we find only the tradition that from ancient times there had been physicians at Salerno. It was not an ecclesiastical foundation, for the names of Jews and of women occur among the earlier teachers; nor was it, as has been supposed, founded by the Saracens, since the earliest writings of the school are free from Arabian influence. In some obscure way the school was a survival of the old Græco-Roman medicine. Its earliest surviving productions are the works of certain Masters—Gariopontus (tenth and eleventh century) and Petrocellus (eleventh century), who were known to the latest Anglo-Saxon writers of the twelfth century. Their works are entirely practical and therapeutical. They contain quotations, generally very inaccurate, from Hippocrates and other Greek writers, with Greek names of diseases (wrongly spelt), but seem to be chiefly based on Latin translations. There is no evidence of borrowing from Arabian writers beyond one or two anatomical terms (which may have been inserted later), and, as a rule, these works are free from charms and superstitious medicine.

This was the first period of Salernitan medicine. In the middle of the eleventh century a great change was produced by the introduction of Latin translations of the works of Arabian physicians, which from this time on were the main foundation of the medicine of Salerno. The earliest of these translations were due to the travelled monk Constantine, who finally settled down in the monastery of Monte Cassino, but lived about 1050 at Salerno. His medical works were entirely based on those of the Arabians, though he did not always acknowledge his debt. He also translated some writings of Hippocrates and Galen from Arabic into Latin. The work of translation was carried on by Christian scholars in the Spanish seats of Mohammedan learning, notably at Toledo by Gerard of Cremona (twelfth century) and others. They turned the Arabic versions of the Greek medical classics, and also many of the original works of the Arabians, into Latin. By their agency a large proportion of the Greek and Arabic medical classics were by the middle of the twelfth century made accessible to scholars throughout Europe. In this strange fashion were Hippocrates and Galen brought back into the European world.

Arabian Medicine.—As the Arabian medicine was for some centuries the dominating factor in European medicine, it seems necessary to give a short sketch of what it actually meant. The medicine of the Arabs, like their science and philosophy, was wholly unoriginal, being based upon the Greek writers, of whose works a large proportion were translated into Arabic. The Arabs studied these works ardently and profoundly, but in a spirit very different from that of their teachers. The Greeks had no dogma, but the Mohammedan Arabs were essentially dogmatic. As their religion was based on the infallible utterances of the Prophet, they treated with like, though unequal reverence the works of the ancient sages. They seem to have had great powers of reasoning and calculation, but their faculty of observation was not so strong; so that their works on Natural History were inferior to what they produced in

other branches of Science. They collected vast libraries, but few museums of natural objects. Their method of advancing knowledge was by deduction and dialectic, more than by induction from observed phenomena. All these qualities had a great influence on European thought and science in the Middle Ages.

But dogma and tradition were not everything with the Arabs. So keen-witted a people could not copy and compile without adding something of their own. They recognised and described new diseases, such as small-pox and measles, unknown to the Greeks, and gave much better accounts of some known diseases, as leprosy and affections of the skin. In Pharmacy they made great advances, introducing new drugs from the East, and new methods, such as distillation. Medieval pharmacy was chiefly Arabian; a part only being derived through the Arabs from the Greeks. At a much later time, when in the sixteenth century the books called Pharmacopœias were first compiled, they were chiefly based on the Arabian writers, Serapion, Mesua, and their followers. To this day, the British Pharmacopœia contains fragments of Arabian pharmacy. Alchemy, though a very old study, was reintroduced by the Arabs, and in Alchemy, with all its faults, lay the germ of modern chemistry. Their anatomy was a mere compilation from Galen and Aristotle, since dissection was forbidden on religious grounds. Astrology, introduced by the Arabs, was a baneful gift to medicine.

The dogmatic spirit of Arabian medicine and science had, no doubt, the effect of reinforcing the similar tendencies which were inherent in medieval thought; and the subtle dialectic in which the Arabs delighted was most injuriously applied to physical subjects. But on one point credit must be given to the Arabs, that they did not countenance superstition, for there are no charms or magical rites in their medical classics. No doubt the secular and rational tone of the Arabian physicians was antagonistic equally to the Oriental Magic and to the miraculous cures of the Christian ecclesiastics; and to them must be mainly ascribed the gradual banishment of these superstitious elements from the regular practice of medicine in Europe.

With all its defects, the Arabian medicine was so far above the level of the European schools in the twelfth and thirteenth centuries, that it gained a complete supremacy. The old Latin tradition, mingled with superstition and folk-lore, disappeared before it. Till the revival of learning in the fifteenth century, and even longer, the practical medicine of Europe was that which the Arabian physicians handed on from their Greek masters. Even the introduction of printing rather helped than hindered its spread; for the works of the Arabian school were more popular and widely diffused than those of the Greeks, whether in the original or in Latin versions. The *Canon* of Avicenna, a manual of medicine, arranged with wonderful subtilty and power of analysis, but in a manner most repugnant to the modern mind, went through numerous printed editions, and held its ground till the seventeenth century. Razes was known by his treatise called *Almansor*

(ad Almansorem), of which the ninth book, separately printed, was one of the most popular of text-books. The works of Serapion and Mesua (including the dubious *Mesua junior*) were the foundation of pharmaceutical knowledge. Abul Kasim (Albucasis), who revived the surgery of Paulus Ægineta, was for a long time the great surgical authority. Averroës, the commentator of Aristotle, helped to give medicine scholastic precision. These were for centuries the chief European medical authorities.

The Scholastic Period.—The time, extending roughly from the twelfth to the beginning of the sixteenth century, during which the Arabian medicine expounded by the original masters or by their followers prevailed in Europe, may be called the Scholastic period. It was not a mere coincidence that the scholastic philosophy reigned in other fields of thought. The same standards, the same methods prevailed in all subjects. The ultimate appeal was to authority and dogma; the method of advancing knowledge was by dialectical reasoning. And whatever may have been the case in Philosophy, there can be no doubt that in physical science and medicine, the syllogism was not only an ineffectual instrument, but actually a hindrance to progress. To reason, however subtilely, from unverified premises, is a very different thing from the verification of hypotheses by induction. The University teaching of medicine was entirely dogmatic and verbal; the favourite text-books mere compilations from the Arabian writers, and from such of the Greek classics as were translated into Latin, composed by the Neoterics or Arabists, as the followers of the Arabian school were termed. The first general text-book, aiming at a synthesis of the Salernitan and Arabian medicine, was the *Compendium Medicinæ* of Gilbertus Anglicus, written shortly after 1200 A.D., a cumbrous collection of theory and practice, mingled with superstitious charms, and containing a vast array of pharmaceutical preparations. Bernard of Gordon, after many years' teaching in the University of Montpellier, brought out in 1306 his *Lilium Medicinæ*, a text-book for students, which owes a good deal to Gilbert's Compendium, but is much better arranged and better written, containing also some original clinical observations. The *Rosa Anglica* of John of Gaddesden, Fellow of Merton College, Oxford, written towards the end of the fourteenth century, is largely based upon Gilbert. It shows some individuality, but contains many absurdities, being disfigured by a recurrence to charms and superstitious medicine; a feature for which it incurred a severe censure from Gaddesden's contemporary, the French surgeon, Guy de Chauliac. These are favourable specimens of the medieval text-books of medicine, which, known by such names as *Practica*, *Aggregator* (*i.e.* compiler), *Conciliator*, and the like, had an immense popularity.

In the fifteenth century some advance was made by the production of what was called *Consilia* (= consultations), that is, clinical histories derived from actual experience, with comments. Among these the works of Bartholomæus Montagnana (died 1460) and Baverius de Baveriis

(died 1480) deserve especial mention. They may still be read with interest. The similar work of Antonio de Benivieni or Benivenius (about 1490), called *De Abditis Causis*, marks a further advance, because the histories are often accompanied by records of the *post-mortem* appearances. His work consists of simple objective observations without speculative explanations.

The Revival of Anatomy.—No truly original point of view can be discovered in any of the above-named writers. The great advances in medicine have generally resulted, not from direct endeavours to improve the art, as practical men suppose, but from some external influence, often from some great movement in science or philosophy. The first step towards the liberation of medicine from the rule of authority, was the introduction of actual dissection into the teaching of anatomy in place of mere dogmatic statements taken from Galen or Avicenna. This was done by Mondino de Luzzi (Mundinus) in the University of Padua about 1310. The new method met with no opposition (for the supposed prohibition of human dissection by the Pope rests on a historical error), but the results were, no doubt, disappointing. Mondino's endeavour was to verify on the human body the statements of Galen. But this was not always possible, partly because Galen's observations had been made on the lower animals, and also because the medieval anatomists had got hold of the wrong book, for Galen's great treatise on dissection (*De Anatomicis Administrationibus*) was unknown to them. In Mondino's text-book of anatomy, which was widely circulated before and after the invention of printing, it is difficult to discover any real advance in anatomical knowledge. Even two centuries after Mondino, his successor in the chair of Anatomy at Padua, Berengarius of Carpi, who re-edited Mondino's text-book, still showed how much his descriptions were biassed by the tradition of Galen. So difficult is it for mèn to see nature with their own eyes! Nevertheless, it was slowly borne in upon the medieval mind that there were other ways of arriving at truth beside authority and reasoning.

The Revival of Learning.—The great movement known as the Renaissance or Revival of Learning can be considered here only as regards its influence on medicine. It influenced our science in many ways. First by the revival of the Greek medical classics in the original, which, though these writers had been imperfectly and in very inaccurate versions known before, was found to breathe a new spirit into medical learning. Next by the invention of printing, which came at the right time to permit the works rediscovered by scholars to be widely distributed. But above all by the renewal of intellectual activity, the bold challenging of authority, the spirit of inquiry and research, which were the distinguishing marks of the New Learning. Moreover, the new scientific methods found new objects to work upon, which the old systems were incompetent to explain. The epidemics of Plague, which had ravaged Europe since the Black Death of the fourteenth century, their contagiosity, their conveyance from place to place,

suggested problems which the ancient medicine could not solve, and indeed had hardly raised. The terrible new disease syphilis which came into prominence about 1490 was something unknown to Hippocrates and Galen, about which the ancient oracles were consulted in vain. The English Sweat, or sweating sickness, of the sixteenth century was equally a new disease unexplained by the doctrines of the ancients. Also the exanthematic Typhus (called at first the Hungarian Fever), which travelled up from the East in the sixteenth century, was a novelty to European physicians of that time.

To deal with these several factors of change in order, we begin with the revival of the Greek medical classics. Among the Greek manuscripts brought into Italy after the taking of Constantinople by the Turks, were probably some copies of Hippocrates and Galen, while other codices were discovered in the European libraries. To make these accessible to the learned world by turning them into pure Latin was the aim of a body of men who may be called the *Medical Humanists.* These men were physicians, and at the same time Greek scholars, but, on the whole, the element of scholarship predominated. Among them were Leoniceno of Vicenza, Winter (Guinterius) of Andernach, Copus of Paris, and, not the least eminent, our countryman Thomas Linacre, whose translations of Galen were by the unanimous verdict of scholars regarded as the most accurate and the purest in style. Rabelais, the great wit and scholar, and Servetus should be added to the list. By the labours of the Medical Humanists, the works of Galen (who was chiefly honoured), Hippocrates, Dioscorides, and other medical classics were turned into Latin, and in the course of time the original Greek texts were also printed, chiefly by the Aldine press of Venice. The rediscovered work of Celsus was also printed in numerous editions.

The hope which animated the Medical Humanists, that when once the pure fountains of Greek medicine (as they phrased it) were reopened the barbarous medieval medicine would be swept away, was not immediately realised. Medical practice was at first little affected, the new Galenism being found to be as dogmatic as the old; and the Greek classics, whether in the original or in translations, were not easily grasped by the mass of the profession, who preferred their old Arabist text-books. But the final downfall of authority came from the revival of physical science, especially anatomy and botany. The revival of the more important works of Galen gave a great impetus to the study of anatomy. The great reformer of anatomy, Vesalius, was a profound Greek scholar, and read Galen's works in the manuscripts, as his friend John Caius informs us. He paid special attention to Galen's great work on dissection, which he himself helped to translate into Latin. When appointed Professor of Anatomy at Padua he diligently set himself to test Galen's descriptions by actual dissection, and gradually found that Galen was incorrect in numerous particulars, because his account had been based on the dissection of apes, not of the human subject. When Vesalius published in 1543 his great work on

The Fabric of the Human Body, illustrated with the splendid woodcuts designed by Jean van Calcar, the supposed infallibility of the great dictator of the medical world was finally exploded. And with this blow to the authority of Galen, an equally severe blow was given to the general principle of authority in science. The science of botany also received new life from the study of the great Greek botanist Dioscorides. The German physicians, to whom the revival of botany was due,—Brunfels, Fuchs, Bock, and Gesner,—were all of them good Greek scholars (and all, it may be remarked in passing, were Protestants). They brought the descriptions of Dioscorides to the test by original study, and by figures drawn from the life of their own indigenous plants. The fine works of the Italian botanist Mattioli were entirely based on the descriptions of Dioscorides, confirmed by actual study of nature.

The great work of placing these two ancillary medical sciences on a basis of positive knowledge was not only important in itself, but of the highest value to the practice of medicine. Gradually the same principles of objective research and careful verification were applied to the study of disease, and with remarkable results. The first step in application of the scientific method to the practical side of medicine was the introduction of the clinical study of patients, combined with the instruction of students.

Da Monti (Montanus), Professor of Medicine at Padua and colleague of Vesalius, gave clinical instruction in the hospital of St. Francis, and attracted a crowd of students from all parts of Europe, among whom was, it would seem, our countryman John Caius, who himself gave an example of the new method of studying disease in his works on the sweating sickness. Da Monti was a humanist and Greek scholar, and himself translated some works of Galen into Latin. In this we see how the Greek revival led to progress in practical medicine as well as in the allied sciences.

The study of new diseases, already referred to, was also greatly influenced by the new and independent spirit which has been introduced into medicine. Among the investigators of syphilis we can here only mention Nicola Leoniceno of Vicenza, the Greek scholar, and Girolamo Fracastori, a brilliant scholar and poet, as well as an original physician, who put his observations on syphilis into the form of a Latin poem. Fracastori rendered a greater service to medicine by his work on *Contagion and Contagious Diseases*. In this he first discussed and formulated the doctrine of contagion, which, except in a few isolated instances, had been strangely passed over by the Arabian and medieval physicians. This work has a permanent value as containing the germ of modern epidemiology.

Paracelsus and the Chemical School.—While the scholars who revived Greek medicine were gradually making head against the supporters of the medieval system, they met in Germany with opposition from an entirely different quarter, namely, from the para-

doxical and cloudy genius known as Paracelsus, whose real name was Theophrastus von Hohenheim (1490-1541). It would be impossible here to give an account of Paracelsus's own system, which was formed on a mystical conception of nature, disease, and remedies, according to which spiritual forces were regarded as essentially controlling the whole material world. We can only notice those points in which it touched other systems and beliefs. Paracelsus was in scientific matters a rebel: he raised the standard of revolt against authority; he trampled the works of Galen and Avicenna under foot literally as well as figuratively, though professing great respect for Hippocrates; and he had naturally no sympathy with the humanists in their revival of Greek medicine. But he was equally opposed to the study of anatomy as giving what he thought materialistic explanations of disease. Being thus in opposition equally to ancient learning and modern science, he put forward his own system as the only guide to progress in medicine. It must be admitted that Paracelsus's revolt against Galenism had some influence in the general breaking up of respect for authority, but this influence does not seem to have spread much beyond Germany and the low countries, though in France it had sufficient force to produce a violent controversy about the use of antimony. For the humoral pathology of the ancients Paracelsus substituted an equally baseless hypothesis, that the fundamental elements of the human body were three principles: *sal*, the solid element; *quicksilver*, the liquid; and *sulphur*, the aerial. This formula was the badge of the Paracelsist school up to the end of the seventeenth century.

Paracelsus must be credited with having a more distinct notion of specific diseases and specific remedies than his contemporaries. The immediate outcome of his hypothesis of specific remedies was the search for *arcana*, the secret principles of drugs, which were to be isolated by extraction and distillation. These endeavours led to the most fruitful part of Paracelsus's work,—his improvements in chemistry and pharmacy. His tinctures and extracts, among which was his *laudanum*, a solid preparation of opium, became famous. He prescribed antimonial medicines, and first introduced the treatment of syphilis by mercury, denouncing guaiacum, which was then the favourite remedy. In surgical pharmacy, the composition of ointments and plasters, he was very successful; the *Emplastrum Paracelsi* was known for centuries.

The usefulness of these remedies formed the strength of the chemical school, composed of the followers of Paracelsus, which may be traced to the end of the seventeenth century. They were distinguished by their employment of the chemical remedies, while the name *Galenical* was given to the old pharmacy. Denounced as quacks by the orthodox school, the chemists came into violent collision with authorities, notably in England with the College of Physicians; but gradually the best parts of the chemical system were fused with the old medicine by such men as Conrad Gesner, Rivière (Riverius) of Montpellier, and Theodore de Mayerne, who settled in England.

In the seventeenth century the chemical school revived in the person of J. B. van Helmont (1578-1648), a chemist of great note, who, though not entirely agreeing with Paracelsus, continued the same line of thought. But the chemical school generally was rather a sort of side-current or back-water than part of the full stream of medical progress.

Medicine in the Seventeenth Century.—Though the centuries do not mark necessarily any distinct divisions in medical history, there is a convenience in following the chronological epochs. At the beginning of the seventeenth century the revived Greek medicine, chiefly Galenical, was firmly established in academies and universities throughout Europe. The chemical school, though discredited in high places, held its ground, and its irregular practitioners must have received a great deal of popular support. There were about this time two movements which require special notice. One was the general adoption in all countries of authorised formularies or pharmacopœias; the other was the rise of experimental physiology, especially distinguished by the great discovery of Harvey.

The introduction of Dispensatories or Pharmacopœias did not properly belong to the seventeenth century, as the first book of this kind was compiled at Nuremberg by Valerius Cordus, 1542,[1] and was followed by similar publications at Lyons, Cologne, and other cities. That of Augsburg, the *Pharmacopœia Augustana*, published 1601, was long regarded as the most authoritative. The object of the old as of modern pharmacopœias was to serve as a basis of understanding between the physicians and the apothecaries, so that the latter might know with certainty what the former meant to prescribe, and the composition of the preparations might be always the same. The *Pharmacopœia Londinensis*, published first in 1618, may be taken as an example of the nature of similar compilations in other countries. It is fully described elsewhere (*vide* p. 258). Pharmacopœias were no doubt useful in maintaining a high standard of accuracy, and improved the practice of Pharmacy. But they had the disadvantage of stereotyping a number of obsolete and useless remedies, which might otherwise have been forgotten.

Some other advances in pharmacology and therapeutics during the seventeenth century must be mentioned. The introduction of cinchona bark as a cure of ague, which was brought from Spain in 1640, not only had its obvious practical utility, but altered the general conception of the action of medicines, as its action could not be explained by the humoral or any other system of pathology, and brought into prominence the conception of a specific remedy for a specific disease. Somewhat later we observe an increased use of opium, partly in new preparations, such as the liquid laudanum of Sydenham. Mercurials were used as remedies for other diseases than syphilis, and various preparations of iron came into use. Chemical remedies, even those not recognised by the pharmacopœia, were increasingly used by regular physicians.

[1] It appears that there was an earlier Pharmacopœia published in Spain in 1535, the *Concordiæ Pharmacopolarum Barcinonensium* of Solano Segundo, a physician of Barcelona.

The Circulation of the Blood.—The great discovery of Harvey, first published to the world in print in the year 1628, though one of the most important events in the history of medicine, does not strictly belong to our present subject, for it had no immediate effect on medical practice. Ultimately the school of experimental physiology which Harvey founded had some share in generating a system of pathology, that of the Mechanical Iatro-physical school; of which a word will be said presently.

But for the first direct application of Harvey's discovery to medicine we must look forward half a century, to the experimental demonstration by Richard Lower at Oxford in 1669 of the production of dropsy by obstructed circulation, a discovery which at once reduced to nothing a vast mass of conjectural pathology on that subject. Christopher Wren first thought of and carried out the injection of medicines into the veins; while Lower, a little later, first performed the operation of transfusion of blood from one animal to another. These achievements of the Oxford school of physiology were direct consequences of Harvey's discovery.

Francis Bacon and the Advancement of Learning.—In the history of medicine the name of Francis Bacon, the first English thinker who had a wide European influence, cannot be passed over. His influence on the progress of medicine, though indirect, was considerable. It has been objected that Bacon's method of induction has not led, and is not likely to lead, to great discoveries in science. This is quite true; but this method, neither understood nor practised by his contemporaries, is precisely that which is followed by the great mass of workers to whom the continuous step-by-step advance of medicine is due. When we record, collect, arrange, and tabulate cases, drawing from them such generalisations as they warrant, we are following the method which Bacon tried to recommend to physicians in his day. He blames physicians for "the discontinuance of that profitable and accurate diligence of Hippocrates, whose custom was to set down a narrative of the special cases of his patients, what the medicament, what the event." A little farther on he emphasises the importance of post-mortem examinations.

Moreover, Bacon's high conception of the aims of science, and his noble enthusiasm for its advancement, were the inspiration of the scientific movement of the seventeenth century, as the founders of the Royal Society of London gratefully acknowledged.

Practical Medicine in the Seventeenth Century.—In the early part of the century the salutary innovation of clinical teaching was introduced into Northern Europe, and first at the hospital of Leyden by Joh. Heurnius and his successor Schrevelius, both pupils of the school of Padua. The Leyden school attained greater renown and popularity under F. de la Boë Sylvius, who became professor in 1658, and attracted a crowd of students from all parts of Europe, England included. His successor, Lucas Schacht, continued the system. In Paris an external polyclinic was founded by Renaudot in 1644; and there was some

clinical teaching at Montpellier. In England we cannot trace any regular clinical teaching, though towards the end of the century young Doctors of Medicine sometimes attended the London hospitals, but even this was not universal.

The medical history of the seventeenth century is largely occupied with the use of two new medical "systems," which were certainly events in the history of medicine, though it may be doubted whether they were steps in its progress.

The Mechanical or *Iatro-physical* School may be said to have owed its origin to the discoveries of Harvey and the mechanical philosophy of Descartes, which led Borelli, Baglivi, and other physiologists to try and find a mechanical explanation of the actions and functions of the body. Borelli, a man of original genius, may be regarded as the founder of the system, which was developed by Pitcairn, a Scottish professor at Leyden, afterwards at Edinburgh. This was, however, mainly a system of physiology; its principles were, indeed, applied to explain the pathology of fevers, but it had little influence on practical medicine, and does not call for further exposition in this place. It was revived in the beginning of the eighteenth century in a more mathematical form.

The *Iatro-chemical* School was the work chiefly of one man, Francis de la Boë Sylvius, already spoken of. He was an excellent anatomist, whose name survives in the anatomy of the brain; and also a good chemist, as chemistry was then understood. His system of pathology referred most diseases to morbid matters, or "acrimonies" produced by perverted secretions, and these being sometimes too alkaline, sometimes too acid, the antithesis of *acid* and *alkali* became the badge- or catch-word of his system. Sylvius does not seem to have extended his system to therapeutics. This system was adopted with modifications by Thomas Willis (1622-75), an eminent investigator of the brain and of nervous diseases, who published his system in a work called *Pharmaceutice Rationalis*, which was influential at the time, but was becoming rapidly forgotten even early in the eighteenth century.

Neither of these schools left any permanent addition to the science of medicine, but by their controversies prepared the way for a method of advancing medicine which attempted to do without general systems altogether.

Some isolated contributions to medicine in the seventeenth century acquire mention. The most notable was the discovery of a new disease —rickets—unknown to ancient or contemporary physicians. This was not discovered by any physician, but by the common people; and the name first appears in the bills of mortality for the city of London, which were not compiled by physicians. It attracted attention early in the century, but the credit of first giving an adequate description of it belongs to Francis Glisson (1597-1677), who published his treatise *De Rhachitide* in 1650. The repeated epidemics of plague gave rise to a new literature on that disease, which is much above the level of that of the preceding century. The best book, on the whole, was that of

Diemerbroeck, *De Peste*, 1646. The plague of London in 1655 was described by a physician, Nathaniel Hodges, in his *Loimologia*, 1666, and by an apothecary, William Boghurst, in his *Loimographia* (not printed till 1894). The apothecary's work is the more valuable of the two. On consumption the works of Bennett and Richard Morton, both of whom refer to the morbid anatomy of the lungs, were important, especially the latter. Willis, already referred to, has left some excellent reports of cases of nervous disease, with accounts of post-mortem appearances, and recognised the presence of sugar in diabetic urine. The study of morbid anatomy became more general. In the *Philosophical Transactions* for 1685 a good figure of cirrhosis of the liver from a case of ascites is given by John Browne, though very badly explained. A large number of post-mortem observations were made in England, Holland, Germany, and elsewhere, but for the most part these observations were of little value, since the anatomists generally regarded the organic changes as consequences of the disease and its symptoms, not as giving rise to them. The most important achievement of morbid anatomy in this century was the discovery by Wepfer of Schaffhausen, published in 1658, that bursting of a blood-vessel in the brain was the usual cause of apoplexy. This simple direct observation at once swept away an immense cloud of hypothesis and speculation on this subject.

The Method of Sydenham.—Sydenham, the greatest physician of the seventeenth century, and one of the greatest in history, must be treated of by himself, because he has no relation to any school or system of his own generation, or of that which preceded it. Influenced, no doubt, he was by the great upheaval of thought due to the Puritan rebellion, and was perhaps always at the bottom of his heart something of a rebel; but he differed from most of the leaders of the scientific movement, such as Glisson, Wharton, and Lower, which began under the Commonwealth, and blossomed out at the Restoration. He took no interest in their researches in physics, anatomy, and physiology, which he regarded as trifling, and he never belonged to the Royal Society. He owed little to education. The medical instruction he received at Oxford must have been of little value, and a few months spent at Montpellier represented all his clinical experience. Ignorance is rarely the parent or even the nurse of originality, but in Sydenham's case it is well to remember how little he was swayed by any academic influences. Among the ancients Hippocrates was the only master whom he acknowledged, and him he took as his model. Among the moderns he speaks with great respect of Bacon as the master of natural knowledge, but of no other leader of science. Of his contemporaries, Robert Boyle alone received his homage, and Sydenham might probably have spoken of himself as a student of nature like Boyle, but in a different field. The main features of Sydenham's method of studying diseases may perhaps be thus stated. First, diseases are objects of natural history which have to be studied by observation alone, without trying to ascertain their remote causes,

and without framing hypotheses. The description of a disease must be complete, including all its features, mere narrations of individual cases being insufficient and unimportant. Diseases have their own natural laws, their own course, their times and seasons. In acute diseases there is a rise or climax and a spontaneous decline. Secondly, nature is the true healer of disease; the physician has to imitate her processes of cure, to aid them if they appear weak, and to moderate them if they are too violent. A disease is, in fact, an effort of nature to expel the morbific matter. In therapeutics, experience is the only test of what is right. Whatever does good is best.

Some of these principles, especially that of the curative power of nature, Sydenham professed to have learnt from Hippocrates, but in minuteness of observation he went far beyond his master. He derived also from Hippocrates his idea of the importance of studying the varied appearances of diseases at successive seasons and years, what he called the epidemic constitution; but too close adherence to Hippocrates sometimes misled him in the matter. Nevertheless, this made him one of the founders of modern epidemiology.

These principles of Sydenham's are evidently more applicable to acute than to chronic diseases, and the former were what he especially studied. All acute inflammations were regarded in the same way as fevers. Sydenham insisted that pneumonia was a general not a local disease—the local inflammation being a part of the general condition. This view was maintained by Skoda of Vienna in the nineteenth century, and is now finding its way into text-books. Sydenham thought anatomy of some, but not of much importance, and he denied that anything could be learnt from examining the body after death. This rejection of morbid anatomy made it difficult for him to explain local diseases, and his accounts of dropsy and of apoplexy are very inadequate. But if this was his weak side, he restored the balance by his admirable accounts of chorea, hysteria, gout, and other diseases in which his unbiassed observation without any special debt to Hippocrates gained some of its greatest triumphs.

In treatment Sydenham must have been very successful. His way of treating small-pox and fevers was spoken of by his contemporaries as a "New Method," and, after much opposition, was in the end pretty generally adopted. It was his great merit that whatever preconceived ideas or hypotheses he might have he was ready to sacrifice them at once at the bidding of experience. Such was "the English Hippocrates" whose independent genius, remarkable insight, and noble character made him one of the greatest master-builders of modern medicine. Sydenham's method in practice may be taken as summed up in the words of his friend and ally John Locke: "You cannot imagine how far a little observation carefully made by a man not tied up to the four humours (Galen) or sal, sulphur and mercury (Paracelsus), or to acid and alcali (Sylvius and Willis), which has of late prevailed, will carry a man in the curing of

diseases though very stubborn and dangerous; and that with very little and common things, and almost no medicine at all."

The Eighteenth Century.—In the great century of "enlightenment" various influences promoted the advance of medicine, but till the latter part of the century there was no great change in principles or methods. The most important factors of advance were the organisation of medical teaching all over Europe, the rise of morbid anatomy to the position of a science, and the elucidation of a number of special diseases due to these improvements. The eighteenth century also produced its general systems which will require brief notice.

At the beginning of the century the great advances in mathematics and astronomy led to attempts at explaining physiology and pathology by mathematical reasoning; producing a modified revival of the Iatro-physical school. This was chiefly the work of Pitcairn at Edinburgh, Keill, Mead, and Freind in London. The English physicians did not let their principles influence their practice, and the new mathematical school had only a temporary vogue. But while it lasted it somewhat hindered the general adoption of the methods of Sydenham.

The impulse to the improvement of clinical teaching came from Hermann Boerhaave (1668-1738), a man of no striking originality, but a very great teacher. He based his teaching avowedly on the methods of Hippocrates and Sydenham, whom he regarded with great and almost equal veneration, but he aimed at uniting with their principles the results of recent anatomical and physiological science, together with a critical study of the medical classics. Boerhaave to his credit propounded no system, and founded no definite school; but his power as a teacher in the promotion of medicine throughout Europe was probably greater than that of any other teacher whose work is recorded. The little hospital at Leyden became the centre of European medicine. Among his pupils were Haller, the great pioneer in physiology, van Swieten and de Haen, the founders of the Vienna School, with many English and Scottish physicians. His influence on English medicine in the first half of the century was paramount, and contributed much to raising the reputation of Sydenham in his own country. The example of organised clinical teaching was followed at Rome in 1715, at Edinburgh in 1746, and at Vienna in 1753. The latter school succeeded Leyden as the chief centre of clinical teaching in Europe, and was regarded as "the pattern of all clinical schools." In England there was no systematic clinical instruction then or for long afterwards, but the custom of attending the London hospitals of St. Thomas and St. Bartholomew became more general; and these hospitals, as also those of later foundation, became informally something like imperfect schools of medicine. Anatomy and surgery, however, were the subjects chiefly studied. In Edinburgh the excellent clinical teaching and the influence of many eminent teachers in all departments of medicine raised the school to the height of prosperity, so that for some generations it was the centre of medical education in Great Britain.

The Rise of Morbid Anatomy.—In addition to the recording of isolated post-mortem examinations, an attempt had been made to collect a large number of observations by Théophile Bonet of Geneva (1620-1689), who published his *Sepulcretum Anatomicum* in 1679 (second edition, 1700). This was a large collection of histories of cases with the appearances after death; a combination which the author held to be the true foundation of genuine pathology and sound nosology. It contained many observations, few deductions, and had little immediate effect. There was an interval of sixty years before the classical work of John Baptist Morgagni (1682-1771), *De Sedibus et Causis morborum per Anatomen indagatis*, appeared in 1761. Morgagni was already seventy-nine years old, having been some fifty years professor of anatomy and medicine, and possessing a European reputation. The book is not a treatise on morbid anatomy in our sense. It consists of a series of letters giving histories of cases with post-mortems, chiefly drawn from the author's own experience and that of his friend Valsalva, with a few borrowed from Bonet, and enriched by copious comments. The immediate effect of Morgagni's work was very great, and it was soon, notwithstanding its bulk, translated into several languages. This effect cannot be ascribed to the great fund of knowledge contained in the book, nor to the eminence of the author, but to the new direction which it gave to the minds of physicians. Attention was concentrated on the seat of disease and on the local changes. In the words of Virchow, "Das anatomische Denken"—"the anatomical way of thinking"—was introduced into medicine, and the construction of a science of pathological anatomy became possible.

The first actual treatise on morbid anatomy, founded on original observation, was the work of Matthew Baillie (1761-1823), nephew of the Hunters, and after his brother John, William Hunter's greatest pupil. William Hunter had begun to form a museum of pathological specimens, which Baillie added to, and on which he based his small but important book, *The Morbid Anatomy of the most Important Organs of the Human Body*, published in 1793. It had an immediate success, and was translated into several languages. The book consists entirely of original observations told in simple language without clinical histories, and without any hypotheses. Baillie supplemented this work by his fine collection of figures, "A Series of Engravings to illustrate Morbid Anatomy," which also was the first of its kind in Europe. Baillie soon became too much immersed in practice to continue his pathological researches, but he carried his knowledge into practice, for it was remarked by his contemporary, Sir Henry Halford, that Baillie's aim in diagnosis seemed to be to ascertain the actual seat of disease and the condition of diseased organs—he aimed in fact at *Physical Diagnosis*, which was to receive in the next century an unlooked-for extension, but at that time was rightly regarded as something new. The new science of morbid anatomy was actively pursued by numerous observers in Britain, Germany, France, and Italy, so that at the end of the eighteenth

and the beginning of the next century it was the most important feature in medical progress. It should not be forgotten that the example and discoveries of John Hunter, the great surgeon, whose work does not come under consideration here, had a powerful effect in advancing morbid anatomy, and leading to the recognition of positive anatomical medicine.

The study of morbid anatomy was the necessary complement to the method of Sydenham, and it is to the combination of the method of Sydenham with the method of Morgagni that modern medicine owes its scientific and progressive character.

Some account must be given of the chief speculative systems of medicine which had their rise and also their decline and fall in the eighteenth century. Friedrich Hoffmann (1660-1742), professor of medicine at Halle, constructed a system which like that of the ancient philosophers rested on a theory of the universe. He supposed life to be a universally diffused ether, which, entering the animal body, became transformed in the brain into the *pneuma* or nervous fluid. Further, he held that health depended upon the maintenance of a proper *tonus* in the body. If this was in excess it produced "spasm," which was the cause of certain diseases; if deficient, "atony" resulted, which caused another class of diseases. Hoffmann was more successful in therapeutics, and introduced some valuable chemical medicines; but kept the composition of some of these secret.

George Ernest Stahl (1660-1734) was a colleague of Hoffmann at Halle, known in chemistry as the inventor of the conception of *Phlogiston*; but his chemistry had nothing to do with his medical system, which was chiefly intended to combat materialism. Its chief feature was the hypothesis of Animism, which attributed to the soul of man the control of the functions of ordinary animal life. The symptoms of disease were regarded as the conscious efforts of the soul to overcome the morbid influences.

One cannot but see that the academical position of these writers and the professorial system had, beside the German love of philosophy, much to do with the genesis of their systems. In England the absence of the professorial system, combined with national characteristics, will explain why no general system of medicine ever arose or took much root in this country; but in Scotland, where the system of medical teaching was more like that of Germany, and where philosophy has never lacked her votaries, it was very different. William Cullen (1712-90), professor at Edinburgh, a very great and successful teacher, propounded a new system of medicine, intended to reconcile the opposing views of his predecessors. Its main feature was the importance attached to the nervous system in the causation of disease. Cullen's *First Lines of the Practice of Physic* was one of the most popular text-books ever published, and for many years the theoretical guide of the British practitioner. The system-building tendency of the eighteenth century did not exhaust itself, however, till it had produced two other general systems. The

so-called "Brunonian" system of John Brown, based on the doctrine of "stimulus," had a meteoric success on the Continent, which it is difficult to understand. The last of the systems was that of Hahnemann (Homœopathy), which we have no space to expound or to criticise.

Vaccination.—At the close of the century Edward Jenner introduced the method of preventing small-pox, which is associated with his name, one of the classical discoveries in medicine. Vaccination is treated of elsewhere (vol. ii.), but it should be said here that, apart from its practical utility, this discovery has been of signal service to the science of pathology by bringing in the idea of immunity to specific diseases, and the means of procuring immunity by introducing into the body a weakened or altered form of the virus producing the disease. The significance of this vast subject is increasing day by day, and modern investigators must look back to Jenner as the originator of their methods. Nor should it be forgotten that in the same year (1761) in which Morgagni's great work appeared, a Viennese physician, Leopold Auenbrügger (1722-1809), published a little book, *Inventum Novum*, in which he gave an account of the method of diagnosis of diseases of the chest by percussion. It attracted little attention, and it was not till revived by Corvisart in the nineteenth century that this valuable invention was introduced into medical practice. The names and works of many other eminent physicians of the eighteenth century must be passed over for want of space.

The Nineteenth Century.—At the beginning of the nineteenth century arose one of the most important movements in the history of European medicine.

The primary impulse was given by the great intellectual upheaval caused by the French Revolution. As at the corresponding period in the seventeenth century in England, a new wave of scientific activity began amidst war and revolution, coming to its height in the peace following the Restoration, and medicine shared the impulse with other sciences. It was the age of Lavoisier and also the age of Xavier Bichat (1771-1802). This remarkable genius, the founder of Histology, made it his aim to find a physical basis in the tissues for normal life, and also in the morbid changes of organs for the processes of disease. All diseases, he held, except the specific fevers and some nervous affections, were to be explained by morbid anatomy. His own short life, full as it was of ardent work, hardly permitted him to do more than touch these subjects, but his ideas were carried out by pupils to whom he communicated his enthusiasm. The school of Bichat was essentially a school of morbid anatomists who were also physicians. Corvisart studied the morbid anatomy of the heart before he introduced Auenbrügger's invention of percussion to the world; G. L. Bayle (1774-1816) may be said to have constructed the pathological anatomy of pulmonary phthisis and of tubercle in other organs. His doctrine of the unity of tubercle, long contradicted, has now been finally established. P. C. A. Louis (1787-1872) carried on the investigation of tubercle, and

first explored the intestinal changes in typhoid fever, and though not actually the discoverer of this disease, he first placed its pathology on a sound basis. His work, published 1829, completely transformed the ideas of the profession on the subject of fevers. Louis also introduced the numerical or statistical method of studying disease, a method which now appears so natural that we wonder it ever required to be invented. Laennec, beside his invention of auscultation, advanced morbid anatomy by numerous important researches; Cruveilhier (1791-1874) later summed up the new science in his text-book and splendid atlas. The new morbid anatomy differed from the old (that of Baillie for instance) not only in being more minute, but in certain new features. One was the introduction of morbid histology, showing how the different tissues of the same organ might be differently affected, and the same tissue in different organs similarly affected in disease. Another new feature was the recognition of the succession of changes, the morbid process in diseases, which first gave a solid foundation for the clinical study of stages of disease. For this science the name Pathological Anatomy was appropriate.

Methods of Physical Diagnosis.—While the morbid changes in organs were being carefully studied after death, no means existed for detecting the same changes during life. This deficiency was supplied by the two momentous inventions of percussion and auscultation. The method of percussion invented by Auenbrügger, already spoken of, was brought into notice by Corvisart in 1808, who coming across the *Novum Inventum*, and being much struck by it, tested the utility of the invention, and translated the book into French without any important additions of his own, very creditably giving all the honour to Auenbrügger. This little book, dealing only with the thorax, described quite correctly the signs given by percussion in various diseases of the lungs, pleura, pericardium, and in enlargement of the heart. Piorry (1794-1879) extended and improved the method of percussion, introducing *mediate* percussion by means of a "plessimeter" in place of Auenbrügger's direct percussion with the tips of the fingers. His treatise *Sur la percussion médiate* appeared in 1828.

The Discovery of Auscultation.—René Théophile Hyacinthe Laennec (1781-1826) introduced a much more important aid to diagnosis than percussion, namely, auscultation. He seems to have made the discovery almost by accident, but at once recognised its importance in ascertaining the condition of the thoracic organs. The information given to the ear by the stethoscope was carefully verified by post-mortem examination, and gradually the connexion between sounds and physical alterations in the lungs was established nearly as we know it now. Laennec demonstrated his method to the Académie de Médecine in 1815, and in 1819 published his classical work *De l'Auscultation médiate*. This was not only a treatise on auscultation, but an account of diseases of the lungs in general, far superior to anything which had preceded it. In respect of diseases of the heart it was less complete. The chief thing which

was afterwards corrected in Laennec's views was his belief that sounds heard in the lung were the "pathognomonic" signs of special diseases, and not as afterwards shown by Skoda, signs of physical conditions which by other evidence are known to accompany special diseases. The discovery of auscultation was closely connected with the study of morbid anatomy, as the present writer has more than once maintained. Candid consideration will show that Laennec's innovation came in the fulness of time, when the way had been prepared for it by the "anatomical way of thinking," without which men would have taken no interest in a means of detecting physical changes in the organs. Had it come earlier it might, at the most, have supplied some empirical rules of practice, but might not have been more fruitful than the scattered hints at auscultation which from the time of Hippocrates to Ambrose Paré, and later, fell on barren ground.

The progress of positive medicine in France was rapid and brilliant. It suffered only one retarding influence, the hypotheses of Broussais, which for some time had immense popularity. Broussais (1772-1838) was deeply impressed with the ideas of Bichat that all diseases, even general diseases, originated in a morbid condition or irritation of particular organs, and ultimately carried this to such an extreme that he regarded all acute diseases as dependent upon inflammation of the stomach and intestines, "gastro-entérite." The symptoms and affections of other parts of the body were derived from this by what he called "irradiation" or sympathy. This one-sided explanation naturally brought him into collision with the pathological anatomists, and only after a long controversy were his opinions finally exploded. But this is only a part of the system called "Broussaisism," which for years was dominant in the French School. In the meantime there was progress in other directions.

An important factor in the advance of medicine was the organisation of clinical teaching. The first important clinical teacher after Laennec himself was A. F. Chomel (1788-1858), who succeeded him at the Charité Hospital; but the greatest of all was Gabriel Andral (1797-1876), who combined the results of pathological anatomy with an exact and refined diagnosis, and summed up the results of his experience in his *Clinique médicale*, published 1829-33, the first book in which the word "clinique" was used in its modern sense. In fact, Andral may almost be said to have first organised clinical medicine in the sense in which we now understand it. The value of the new method was shown by the number of important researches in special branches of medicine, of which we can only allude to a few, such as the work of Bretonneau on diphtheria, of Rostan on softening of the brain, of Albert, Biett, and Rayer on diseases of the skin, of Andral and Gavarret on the blood.

Experimental pathology, the way to which had been shown by John Hunter, formed part of the great work of François Magendie in experimental physiology. His pathological experiments, few as they were, and those on the action of medicines laid the foundation of experimental

research in these fields, which was afterwards widely extended by his brilliant successor Claude Bernard.

English Medicine at the beginning of the Nineteenth Century.—Beside France the only country in which there was any real progress in medicine was England. Germany was involved in the fogs of the "Natur Philosophie," and Italy was given over to the rival systems of Brown and Rasori. The positive tendency in medicine, working by observation and experiment without systems and hypotheses, was natural to the countrymen of Harvey, Sydenham, and Hunter; and the progress of medicine in England was on the whole parallel to that in France; but in the English medical profession there was less enthusiasm for science, and progress was hindered by serious defects in teaching and organisation. The method of Sydenham may be said to have been illustrated in the researches of Willan and Bateman on diseases of the skin, a subject in which the humoral pathology and other hypothetical systems had given play to their wildest fancies, and where the sane observation of the naturalist school was especially needed.

Morbid anatomy made steady progress, and the custom of making post-mortem examinations became more general; but much of the best work in this subject and in the pathology of inflammation was done by surgeons, not by physicians.

A powerful impulse was communicated to English medicine when, after the peace, many British physicians went to study in Paris. The attractions were the admirable clinical teaching, to which there was nothing parallel in this country; the opportunities for studying morbid anatomy, in which subject C. J. B. Williams said he learnt more in eight months at Paris than he could have done in as many years in London; but, above all, the new art of Laennec, in whose class the foreign physicians outnumbered the French students. The stethoscope and its use were brought back to England by pupils of Laennec and others. Forbes (Sir John) translated Laennec's work in 1821, and Auenbrügger's in 1824; Stokes and Graves of Dublin published observations on the subject in 1825-27; and C. J. B. Williams, who has left interesting records of Laennec's practice, brought out an *Exposition of the Signs of Disease of the Lungs* in 1828. The new method of diagnosis in pulmonary diseases thus gradually permeated the profession, but the auscultation of the heart was still very deficient. This subject was investigated by Elliotson of London, and Corrigan of Dublin, whose name is well known in connexion with a particular state of the pulse. The explanation of the natural sounds of the heart also attracted attention, and a controversy arose in which Corrigan, Hope, and Williams took part. Gradually the subject became clearer, but it was long before the physical diagnosis of heart disease was placed on a firm basis.

The study of pathological anatomy in England was stimulated also by the example of the French school. The special researches and discoveries of English observers in this field were numerous and important,

but being scattered through medical journals, transactions of societies, museum catalogues, and the like, not in separate books, it is difficult to sum them up under any general heading. There was no systematic teaching of the subject for many years, and text-books were few. The first English text-book which could compare with the great French works was that of Carswell, published in 1838. The improvement of the microscope greatly assisted the progress of pathological and of normal minute anatomy; so that the construction of the first successful achromatic combination by Joseph Jackson Lister (father of Lord Lister) in 1829 marks a date in the history of medicine. Although anticipating a little, we must here mention the foundation of the Pathological Society of London in 1846, which made an epoch in the study of this subject in England. The transactions of this society contain an immense number of single observations in morbid anatomy, elaborate memoirs and wide generalisations being for the most part excluded. They constitute, in fact, a *museum in print.* About this time it may be noted that the word "pathology" was used as synonymous with pathological anatomy, or even with pathological histology, a usage which has led to confusion, since the corresponding word in other languages is used for the science of disease generally.

To return to the early part of the century. It was by combining the results of morbid anatomy with careful observations of patients in hospitals that the great discoveries of the English school in this period were made. The London hospitals at this time were predominantly surgical, medicine occupying a subordinate place; but it was the special merit of the school of Guy's Hospital to give a more prominent position to medicine and to encourage post-mortem examinations, with notable results to the science of medicine. Its eminent physicians made discoveries with which their names are still associated. Thomas Hodgkin (1798-1866), an excellent morbid anatomist, first described the affection of the lymphatic system called Hodgkin's disease. Richard Bright (1789-1858), combining the chemical examination of urine, which had already been studied by Blackall and Wells, with the clinical study of dropsy and the morbid anatomy of the kidneys, first framed a complete synthesis of chronic inflammation of the kidney, and established as a morbid entity the disease known by his name, one of the great discoveries of the nineteenth century. His colleague, Thomas Addison (1793-1860), a great clinical teacher, discriminated the form of anæmia since called pernicious; and discovered that affection of the adrenals which has made his name most widely known. These men had worthy successors, whom we have no space to mention, but of one of them, Sir Samuel Wilks, we need not, happily, speak in the past tense.

In the next generation the same work of discriminating special diseases and improving the art of diagnosis was carried on in all the medical schools of London by numerous eminent teachers, and also by some who stood outside the schools. We can only refer to the work of Johnson and Dickinson in continuing the researches of Bright, of

Richard Budd on diseases of the liver and typhoid fever, Peacock on diseases of the heart, of Marshall Hall and Lockhart Clarke on diseases of the nervous system; but there were many other equally eminent physicians. If we do not speak of them more fully, it is because no new method and no new principles were introduced till past the middle of the century, unless the increased use of the microscope be regarded as a new method. As has generally been the case in England, these labours were isolated and individual, while the division of teaching among several schools in London prevented any one from attaining a dominant position.

In Edinburgh the traditions of Cullen were maintained by eminent teachers such as James Gregory (1758-1821) and William Pulteney Alison (1790-1859), and by the strong individuality of Hughes Bennett. John Abercrombie was one of the pioneers in investigation of nervous diseases; and Sir Robert Christison, great in several fields, though supreme in none, was one of the pillars of the Edinburgh school.

In Dublin two great physicians maintained a high level of clinical teaching. Robert Graves (1800-1853), whose clinical lectures served as a model to the eminent French teacher Trousseau, is also known as the investigator of exophthalmic goitre. William Stokes (1804-78) followed with undiminished lustre, and has also left his name associated with a morbid condition. In all these centres the progress of medicine was continuous, but not strikingly altered till the introduction of some new ideas and methods from the German school in the second half of the century.

In the meantime an episode, of great importance in the history of fevers, must be noted. When the English pathologists began to test, on the continued fevers of their own country, the results of Louis and the French school on the intestinal lesions of typhoid fever, it was found that in a large proportion of cases these lesions were absent. This arose from the inclusion under one name of the old exanthematic typhus and relapsing fever, as well as what the French called typhoid. The French pathologists really investigated only one of these diseases, because since the Napoleonic wars typhus had been virtually absent from France, and relapsing fever was unknown. Some concluded that these lesions were not essential to continued fever, but found only in some cases. Others inferred that there were really two distinct diseases, viz. typhus and the typhoid of the French (beside the relapsing typhus); other distinctions, especially that of contagiosity, were also noted. The distinction seems to have been first recognised by Gerhard, of Philadelphia, in 1837, who knew the true typhus in his own country, and by other American physicians who had the opportunity of studying fevers both in Paris and in London. This view was also strongly supported by some British physicians, especially by Alexander Stewart, on the strength of his researches in Glasgow and London. But the contrary view of the unity of the typhoid fevers was maintained by eminent men in this country, such as Graves of Dublin, and Christi-

son of Edinburgh. The distinction was at length admitted by Louis in 1841. Professional opinion was not, however, generally convinced on either side of the channel till in the years 1849-51 Jenner (Sir William), by elaborate researches, based on the vast experience of the London Fever Hospital, established the distinction of the two fevers, typhus and typhoid, in clinical course, in morbid anatomy, and in origin, and thus laid this disputed question finally to rest. The great work of Charles Murchison on *The Continued Fevers of Great Britain* summed up the whole subject, and rapidly gained a position of European authority.

The German School.—The reform of medicine in Germany, long delayed by a devotion to philosophical systems, is unanimously ascribed by German writers to the initiative of J. L. Schoenlein, professor at Würtzburg and at Berlin, who, in the words of Haeser, "was the first to establish in Germany the exact method of the French and the English, and to impregnate this method with the vivifying spirit of German research." Schoenlein was little known outside his own country, except for his remarkable discovery that the disease favus was caused by a parasitic fungus, which though seemingly a small matter, led the way to subsequent researches on the parasitic origin of disease. In another field Johannes Müller, the great physiologist, and also the last of the universal anatomists, led the way to a complete pathological histology by his great work on tumours and morbid growths which made an epoch in that subject. His physiological researches also greatly influenced the methods of experimental physiology in the next generation.

The chief centre of practical medicine in German lands was the School of Vienna, which rivalled and ultimately surpassed Paris in European importance. The pathological anatomist, Carl Rokitansky, in his monumental work, introduced a new method into morbid anatomy by a classification of morbid processes, showing the results produced by each in different organs. With this was combined a system of general pathology based upon the doctrine of *morbid crases*, which was destroyed by the cellular pathology. The chief clinical professor was Joseph Skoda, who in his *Abhandlung ueber Perkussion und Auskultation*, the most important contribution to physical diagnosis since Laennec, explained the sounds studied by these methods, not merely as empirical signs, but as instances of definite physical laws. A more brilliant clinical teacher, Johann Oppolzer, who left no important work behind him (for the lectures published under his name represent him very imperfectly), contributed still more to the popularity of the Vienna School.

The Cellular Pathology.—The next great movement in medicine was based upon the great biological discovery of the "cell" and its independent vitality. It is roughly true to connect this discovery with the names of Schwann and Schleiden, but many others, whose names cannot be mentioned here, contributed. Also it should be remarked that the new science of embryology introduced ideas which influenced the doctrine now to be considered. The aim of this new doctrine was

to show that not only processes of life but processes of disease took their origin within the limits of the cell; and thus pathology, like biology, required a new localisation and a new construction. Such ideas were, no doubt, floating in the minds of many pathologists, and not only in Germany; but their synthesis and reduction to a definite doctrine (it would not be fair to say a *system* in the old sense) was due to Rudolf Virchow. The old humoral pathology conceived of the factors of disease as diffused through the body, and settling down on particular parts, so as to cause local diseases; the gross morbid anatomy had shown that diseases might originate in the organs, and, further, according to the fine analysis of Bichat, in the separate tissues; now it was to be shown that the cell itself might be the actual seat of morbid change.

Virchow's scientific activity began with the study of morbid anatomy, and an attempt to extend the positive results of the French and English schools by the inclusion of factors derived from general biology, physiology, and chemistry. To further this aim he founded the *Archiv für pathologische Anatomie*, in 1847, with the assistance of a gifted colleague, Benno Reinhardt, who died young. His activity took two principal lines: one the promotion of minute pathological anatomy; the other the promotion of experimental methods of solving pathological problems. In the former line of research he was followed by a brilliant school of pathologists too numerous to mention. In the second, which owed much to the physiologists, his immediate followers were Traube, Cohnheim, and others. The book called *The Cellular Pathology*, propounding the doctrine mentioned above, was published in 1858, and had an extraordinary effect in altering the point of view of pathologists all over Europe. It transformed the pathological teaching of Vienna, and had great influence in France and England.

In our own country several investigators, such as Goodsir, Hughes Bennett, Lionel Beale, and Sir James Paget, had worked at microscopical pathology, but with inadequate technique and without regular laboratories. Now the superior technical methods of the German school transformed the study, and the new pathological histology was actively prosecuted by pathologists whose names are too recently known to require mention. In France the manual of Cornil and Ranvier was the representative of the new school. The name of Virchow became known everywhere, not only for the cellular doctrine, but for the numerous valuable special researches which this remarkable genius kept on producing, and which we cannot notice here. In the space of some twenty years he had impressed his individuality on a particular phase in the progress of scientific medicine, which may, perhaps, hereafter be known as the period of pathological histology, though during this time the experimental method made almost equal progress.

It is important to observe that the achievements of this period were mainly valuable in explaining the *processes of disease*. The other main division of pathology, the *causes of disease*, awaited its development

by other schools and other methods. The cellular pathology, already corrected in some fundamental points, was not so much destroyed as supplemented by the new doctrine, namely, the demonstration of living causes of specific diseases, called very inadequately the "germ theory," or, later, "bacteriology." Passing over the many important clinical discoveries of the middle and latter part of the nineteenth century, we must give a brief account of this momentous innovation in Pathology.

The Parasitic Origin of Disease.—In the last third of the nineteenth century was gradually developed a doctrine which has profoundly altered the principles of modern medicine, and greatly modified its practice with regard to specific diseases; namely, the belief that such diseases are caused by living organisms, whose life is distinct from that of the diseased body.

It would be impossible even to glance at the researches of naturalists and chemists, apart from medicine, which led up to this great discovery; but, so far as medicine is concerned, its history dates from the discoveries of Louis Pasteur, a chemist not a physician. Pasteur was led to study the process of fermentation, and established, in opposition to the theory of Liebig, that alcoholic fermentation is caused by a living organism—the yeast fungus—and other similar processes, such as putrefaction, by allied organisms or by bacteria. It was also necessary to prove that these organisms were not produced by spontaneous generation, and that the processes in question could not take place when the organisms were absent from the beginning, removed, or killed. These ideas were not absolutely new, but lacked the precise proof which Pasteur supplied. Pasteur was much impressed with the analogy often suggested between the processes of disease and fermentation. Specific febrile diseases had been called *zymotic*, implying the belief that they were caused by a virus like a ferment, but whether such ferments were products of the diseased body or of living organisms was not known, and indeed hardly discussed. After the war of 1870-71, Pasteur was much interested in the views, hinted at by some French surgeons, that the inflammatory processes in wounds were caused by germs, analogous to those of putrefaction, introduced from outside. His views were strengthened by the results of Lord Lister's antiseptic surgery. The great author of this vast reform in surgery, who had himself studied fermentation, *after nine years'* labour in introducing his antiseptic system, expressed in 1874 his gratitude to Pasteur for the latter's brilliant researches on the germ theory of putrefaction, which had furnished him with the principle of the antiseptic system. Thus while Pasteur's principles were the starting-point, it was Lister who, several years before, had applied them to explain the inflammatory and putrid processes arising in wounds. Lister's system had not only that practical importance which the whole world has recognised, but a scientific importance also, because every rigorous Listerian operation was an experiment, demonstrating the truth of the "germ theory" in traumatic inflammation.

Pasteur's own researches were at first directed to the explaining of diseases in animals, the "cholera des poules" and anthrax or splenic fever in cattle and sheep. The bacterium of the latter disease had been observed years before by Davaine and afterwards by Pollender; and experiments in inoculating the disease had been made. Pasteur carried the research a step farther by growing the organism in fluid; but the final isolation of the bacillus was effected by Robert Koch, who first showed the living cause of the disease, growing apart from the body and absolutely purified by successive cultivations from every particle of the original diseased body. This was indeed the first instance of the complete isolation of the living cause of any specific disease. The accurate methods introduced by Koch were the starting-point of the separation and pure cultivation of the microbes of numerous diseases, including tuberculosis and cholera. In the meantime Pasteur entered on an entirely different line of research. Following out the idea of Jenner's vaccination for small-pox, he endeavoured to discover some method of producing a *weakened* virus, which if introduced into the body of the animal might confer *immunity* against the bacillus of anthrax. He succeeded in producing what he called the "vaccine" of anthrax; and by inoculating young sheep with this gave them immunity against the disease for at least two or three years, long enough to rear them so as to be of commercial value. The economic results of this method were very important, but its scientific results have a range which it is difficult to limit, for the modern researches on "immunity" had here their starting-point. Pasteur's method of treating hydrophobia, arrived at by similar researches, was still more remarkable, as the long incubation period of rabies made it possible to convert a method for producing immunity into a method of cure.

The developments of the great Frenchman's discoveries were chiefly in what may be called the dynamical side of bacteriology,—in prophylactic and therapeutic methods. The development of the morphological side, and the discovery of new species of bacteria, have been chiefly due to the German school and their followers. Their refined and precise technical methods were developed into an organised system of research by which most of such discoveries have been made. The most striking of all was the discovery of the bacillus of tuberculosis by Koch in 1882,—the key to a mystery which had perplexed physicians from the very commencement of the medical art, as we know it. It is enough to suggest how such diseases as typhoid fever, diphtheria, pneumonia, plague, with many more, have been explained in the same way; and how the processes of suppuration and septic diseases have been brought under the clear light of science. A combination of Pasteurian ideas with the positive results of modern research has connected practical medicine with the methods of serum diagnosis and serum therapeutics. The value of bacteriology in the study and control of epidemic diseases, in preventive medicine, and in general hygiene is becoming greater every year.

Protozoa as Causes of Specific Diseases.—While the discoveries of

bacteriology refer only to vegetable organisms, it has lately been shown that several animal organisms, belonging to the protozoa, are the cause of specific diseases. It was Laveran, in Algeria, who first detected the *plasmodium malariæ* as a parasite of the human blood corpuscles, and the cause of quartan ague. Since that time the list of malarial parasites has been much added to. The problem how such minute organisms enter and leave the blood has been solved by the discovery that (as first observed by Sir Patrick Manson in the case of the *filaria sanguinis hominis*) they are introduced and also carried away to other victims by certain species of mosquito, which constitute a sort of intermediate host for the parasite. This remarkable discovery of Major Ronald Ross, that malaria is conveyed by mosquitoes, has been the starting-point of a series of researches on other fevers, such as yellow fever, sleeping sickness, kala-azar, and on diseases of animals such as that conveyed by the tsetse fly. In all these some protozoal parasite of the blood is found to be conveyed by an intermediate host in the shape of a mosquito or some species of fly. In one class of diseases of animals, possibly affecting man, a tick (ixodes) is the carrier of the parasite.

The extraordinary and novel field of research thus opened up forms an important part of the study of tropical diseases; and may be regarded as the latest chapter in the history of medicine to which British observers in various parts of the world have largely, not to say chiefly, contributed. Those remarkable laws have been confirmed by the rigorous test of practical utility. For it has been found possible, by means of precautions founded on them, to protect human beings in highly malarious localities; and to diminish, if not to extirpate, intermittent fevers in certain districts. Thus, as in Bacteriology, and in many other instances, the results of minute and refined researches, first regarded as unpractical, have turned out in the end to be more truly practical than empirical maxims drawn from the routine of daily practice.

J. F. Payne.

MEDICAL STATISTICS

By John Tatham, M.A., M.D., F.R.C.P.

Preliminary Remarks; Tuberculosis; Phthisis; Tuberculous Meningitis; Tuberculous Peritonitis; Malignant Disease; Diphtheria and Croup; Enteric Fever; Measles; Scarlet Fever; Small-pox; Chicken-pox; Whooping-cough; Pneumonia; Influenza; Rheumatic Fever; Diabetes Mellitus; Syphilis; General Paralysis of the Insane; Acute Nephritis, Chronic Nephritis, Bright's Disease; Infantile Mortality.

An article on Medical Statistics, in order to be suitable for a Modern System of Medicine, should be, above all things, practical. Among other

individual diseases is thereby implied. It is well known that the incidence, and probably the fatality also, of many of our common maladies is largely determined by what is known as "environment," dwellers in the urban areas suffering more severely than those in the rural. In order to illustrate this point, I have arranged a selection from among the English counties so as to show, in one group, those areas which contain the chief industrial centres and which are therefore mainly urban in character, and in the other group areas either entirely rural or containing a few inconsiderable towns or villages which do not alter the rural character of the population (7). The urban group contains an aggregate population exceeding 18 millions, and the rural group a population of about 4 millions. In the year 1901, on the sure basis of the census figures, the county populations in both these groups were selected with great care, and they are sufficiently numerous to be regarded as fairly representative of English urban and rural populations respectively. For each area I have calculated the male and female mortality from certain of the principal diseases, and have corrected the rates for age differences of the living. The results appear in the tables that follow. Shortly after the census enumeration of 1891 I made a careful investigation of the causes of mortality among men engaged in the chief occupations, utilising for this purpose the enumerated census numbers of the living, and the deaths registered in that year and in the two years respectively preceding and following the census, the ages of the deceased in the several occupations being carefully ascertained (8). The available results will be found in the following pages as the several diseases come under review. Unfortunately, no similar investigation has hitherto been possible as to the causes of industrial mortality amongst women.

Tuberculosis.—Among the definite maladies that afflict mankind in this country the most important statistically are those which modern pathologists regard as infections, and of these the most frequent are the infections by the bacillus of tubercle. At present no reliable information is available as to the extent to which the general population suffers from tuberculosis; consequently, in attempting to estimate the incidence of tuberculous sickness in a given place or at a given time, we have to rely inferentially on the death-roll. But, for the reason that tuberculosis frequently admits of cure, a mere enumeration of fatal cases furnishes at best but a rough measure of the mischief done. Of the numbers slain in conflict with this ruthless destroyer the death-registers give a fairly accurate account; but what of the thousands who, incapacitated for work by its ravages, go to fill our hospitals and our workhouses? The official records show that of the half-million or so of deaths occurring annually in England, not less than 11 per cent are caused by tuberculosis. This terrible sacrifice of human life to the depredations of a clearly suppressible parasite is surely a matter for serious national concern. But not on that account alone does tuberculosis demand exceptional study. There is the further consideration that this disease selects its victims, not from the

physically degenerate only, but from among the choicest of our race—destroying or maiming, in their early prime, thousands of bread-winning parents or guardians, whose lives, if spared, would have been of incalculable value to the community.

The general teaching of English statistics respecting fatal tuberculosis is as follows :—In the year 1854 the deaths from all forms of tuberculosis together constituted about a seventh part of the deaths from all causes, which latter were in the proportion of 22·5 per thousand of the population. Half a century later, namely, in 1903, the general death-rate had fallen to 15·4 per thousand, and of these only a ninth part resulted from tuberculosis. In the decennium 1851-60 the sexes were affected in about equal proportions, but in 1891-1900 the mortality of females did not exceed four-fifths of that of males.

At certain stages of life the incidence of mortality varies enormously. For example, in the decennium last completed we find that whilst among children under five years the proportion of deaths from tuberculous affections did not exceed 7 per cent of the deaths from all causes, the proportion at the ages 15-35 years amounted to 37 per cent.

In the following table, which relates to England and Wales, the average death-rates per thousand living at several ages, from the principal forms of tuberculosis, are shown for the years 1901-3 :—

MALES.

	All Ages.	Under Five Years.	5-	10-	15-	20-	25-	35-	45-	55-	65-	75-
Tuberculosis, all forms	2·03	3·44	·66	·46	0·99	1·81	2·32	2·94	3·27	2·71	1·75	·67
Phthisis	1·46	·36	·15	·17	·77	1·59	2·13	2·77	3·09	2·52	1·60	·58
Tuberculous meningitis	·20	1·17	·29	·12	·06	·04	·03	·02	·02	·01	·01	·00
Tuberculous peritonitis	·19	1·23	·10	·07	·05	·04	·03	·03	·03	·04	·02	·01
Generalised tuberculosis	·13	·60	·08	·06	·07	·08	·08	·08	·08	·08	·04	·02
Other tuberculous affections	·05	·08	·04	·04	·04	·06	·05	·04	·05	·06	·08	·06

FEMALES.

	All Ages.	Under Five Years.	5-	10-	15-	20-	25-	35-	45-	55-	65-	75-
Tuberculosis, all forms	1·51	2·91	·69	·70	1·23	1·43	1·74	1·95	1·59	1·24	·93	·45
Phthisis	1·02	·32	·20	·40	·97	1·24	1·57	1·79	1·45	1·11	·81	·33
Tuberculous meningitis	·17	1·04	·26	·13	·07	·04	·02	·02	·01	·00	·00	·00
Tuberculous peritonitis	·16	·98	·11	·07	·06	·05	·05	·04	·04	·03	·02	·01
Generalised tuberculosis	·12	·52	·09	·07	·09	·06	·07	·06	·05	·05	·04	·03
Other tuberculous affections	·04	·05	·03	·03	·04	·04	·03	·04	·04	·05	·06	·08

BOTH SEXES.

	All Ages.	Under Five Years.	5-	10-	15-	20-	25-	35-	45-	55-	65-	75-
Tuberculosis, all forms	1·76	3·18	·67	·58	1·11	1·61	2·01	2·43	2·39	1·93	1·29	·54
Phthisis	1·23	·34	·17	·29	·87	1·41	1·83	2·26	2·24	1·77	1·16	·43
Tuberculous meningitis	·19	1·10	·27	·12	·07	·04	·03	·02	·01	·01	·00	·00
Tuberculous peritonitis	·17	1·11	·10	·07	·05	·04	·04	·04	·04	·03	·02	·01
Generalised tuberculosis	·12	·56	·09	·06	·08	·07	·07	·07	·06	·07	·04	·02
Other tuberculous affections	·05	·07	·04	·04	·04	·05	·04	·04	·04	·05	·07	·08

From this table it appears that tuberculosis falls most heavily on young children, the mortality within the first five years of life, chiefly from the abdominal and cerebral forms of the disease, being at the rate of 3·18 per thousand living at that age. After the fifth year the mortality falls

suddenly, and in the two succeeding quinquennial periods averages considerably less than one per thousand. After the stage of puberty the rate again rises, and in the period 20-25 years is equal to 1·61 per thousand. Subsequently it still further increases, reaching its maximum at the age 45-55 for men, and ten years earlier for women. From thence onwards to the close of life the death-rate in both sexes steadily declines. The mortality begins to increase at an earlier age in girls than in boys, and after the attainment of its maximum the fall is most rapid in men.

Phthisis.—A glance at the last table indicates that among the diseases of the tuberculous group by far the most destructive is phthisis—at least 120,000 lives having been sacrificed to that affection within the last three years. The term "phthisis" is generally considered synonymous with pulmonary tuberculosis, and at the present day it is probable that most of the deaths referred to phthisis are actually due to specific infection. This, however, has not always been the case, especially in some remote parts of the country, where at one time all lung affections attended with wasting and expectoration were put down to "consumption" or "decline"—the common equivalents for phthisis. However, it is satisfactory to know that either the term tuberculous phthisis, or its synonym, pulmonary tuberculosis, is now generally used in place of the indefinite names referred to. It is in the interval between the fifteenth and the seventy-fifth year that the chief loss of life from phthisis takes place; few deaths occurring during the periods of infancy and extreme old age. The table shows that among young children phthisis mortality is low, averaging not more than thirty-four deaths in a hundred thousand living under the age of five years, the rate between five and ten years averaging only seventeen in the same number living at that age. In both sexes it is with the approach of puberty that the chief liability to death from phthisis occurs; this liability beginning somewhat earlier in girls than in boys. The maximum mortality is reached at the age 35-45 among women, and ten years later, namely, at 45-55, among men, at which ages respectively the death-rates are 1·79 and 3·09 per thousand. This subject will be further considered presently. According to English experience, females are somewhat *less liable* than males to succumb to phthisis at ages under five years, considerably *more liable* at ages from five years to twenty, and *less liable* at subsequent ages. In the course of the last half-century the saving of life due to reduction of phthisis fatality has been remarkable—this disease contrasting strongly in that respect with cancer, which, on the contrary, has exhibited throughout the same period a steadily increasing mortality. In proportion to the living at all ages, phthisis now destroys, in each year, less than half the number that succumbed to it annually half a century ago. In the year 1903 the phthisis death-rate of females was only one-third of what it had been in 1854, and that of males little more than half. In order to show the variations in phthisis fatality at the several ages during the last forty years, I have prepared the following table, in which the death-rates have been corrected by

assuming the same age composition of the population throughout the four decennia. The corrected rates indicate a greater reduction in phthisis mortality than would the uncorrected or "crude" rates :—

Ages.	Males.				Females.			
	1861-70.	1871-80.	1881-90.	1891-1900.	1861-70.	1871-80.	1881-90.	1891-1900.
All ages	2·54	2·29	1·90	1·58	2·55	2·10	1·66	1·21
0-	·99	·79	·55	·44	·95	·75	·52	·39
5-	·43	·34	·25	·17	·48	·38	·33	·24
10-	·61	·48	·34	·23	1·05	·85	·70	·50
15-	2·20	1·69	1·29	1·00	3·12	2·41	1·81	1·29
20-	3·89	3·11	2·34	1·89	3·97	3·15	2·33	1·59
25-	4·11	3·71	3·04	2·37	4·40	3·56	2·80	1·92
35-	4·17	4·14	3·58	3·10	3·91	3·41	2·74	2·12
45-	3·88	3·87	3·51	3·14	2·87	2·47	2·06	1·64
55-	3·31	3·21	2·92	2·62	2·08	1·79	1·52	1·24
65-	2·04	1·93	1·82	1·58	1·25	1·10	·98	·81
75-	·66	·60	·69	·56	·45	·41	·40	·35

This table shows that the several stages of life in each sex have participated in the reduction of phthisis fatality. In every case the mortality in the later period has been lower than in the earlier, but the rate of decrease has varied widely, and has been generally greater in females than in males. Among persons of both sexes below the age of 25 years phthisis mortality has fallen, on the average, by from 50 to about 60 per cent. From the age of 25 onwards to the close of life the fall has been considerably less marked ; its incidence has been exceptionally favourable to the female sex. The reduction indicated in the table may not be wholly real, but may depend in part on a vaguer statement of death-causes in the earlier period. The habitual use in some districts of the terms "consumption" and "decline" to describe any lingering disease of the lungs has been already referred to.

The following table shows the changes that have taken place in the age of maximum mortality from phthisis in the course of the last half-century ; in each period the age of absolute maximum is indicated by heavy type, the other ages being approximate :—

Periods.	Males	Females.
1851-60	**20-25**, 25-35, 35-45	**25-35**
1861-70	25-35, **35-45**	**25-35**
1871-80	**35-45**	**25-35**
1881-85	**35-45**	**25-35**
1886-90	35-45, **45-55**	25-35, **35-45**
1891-95	**35-45**, 45-55	**35-45**
1896-1900	35-45, **45-55**	**35-45**
1901-3	**45-55**	**35-45**

Tracing back the age of maximum mortality from phthisis, we find that it has not always been as it is at present: in both sexes the age has been postponed. In the decennium 1851-60 the maximum death-rate among females was 4·58 per 1000, and occurred at the age 25-35; the maximum among males was practically maintained through the age-groups 20-25, 25-35, and 35-45, ranging only between 4·00 and 4·05 per 1000 at these ages. In 1851-60, therefore, the maximum mortality was 13 per cent greater among females than among males. In 1901-3, on the other hand, the maximum mortality of males occurred at the age 45-55, the rate being 3·09 per 1000; among females the maximum occurred ten years earlier, being 1·79 per 1000, or less by ·42 per cent than the maximum rate among males. It will thus be seen that the relation of phthisis mortality to sex has been reversed in the course of the last half-century.

The subjoined table, which relates to the years 1899-1903, is intended to contrast the phthisis mortality incidental to town life with that prevailing among dwellers in the country: the figures denote corrected average rates at all ages in each thousand of the respective populations.

	Males.	Females.	Both Sexes.
Urban counties	1·67	1·11	1·38
Rural counties	1·26	1·06	1·16
England and Wales	1·50	1·06	1·27

It thus appears that in the period above specified the same number of persons of both sexes among whom 100 deaths from phthisis occurred in the rural group of counties, furnished 119 deaths in the urban. As regards susceptibility to fatal infection by tuberculosis, the conditions of town life would appear to be most detrimental to the male sex; for whereas the difference in the rates of urban and rural phthisis mortality was 33 per cent for males, it was only 5 per cent for females.

Unfortunately, the industrial mortality from phthisis in women has not as yet been ascertained; but in men it varies enormously in the several occupations. The following list shows the phthisis mortality of males aged 25-65 years that prevailed in 1890-92 in some of the English industries, compared with the mortality of "Farmers," the latter taken as 100:—

Farmers	100*
Tin-miner	643*
Innkeeper (London)	567
Costermonger	561*
File-maker	509
Cutler	484
Lead-miner	481
Potter	422*
Copper-miner	419
Printer	413*
Dock labourer	411
Messenger, porter	411
Agricultural labourer	146
Fisherman	144
Gardener	142*
Schoolmaster	141
Miner	138
Coal-miner (Durham)	119*
Ironstone-miner	114*
Artisan	111
Coal-miner (Staffs.)	105*
Railway engine-driver	96
Coal-miner (Derby)	87*

These figures are sufficiently striking. It should, however, be added that in those industries in the foregoing list marked by an asterisk the mortality from phthisis in 1890-92 was lower than it had been in 1880-82.

From returns furnished to the English Registrar-General by the Presidents of the Statistical Bureaux of several foreign countries, and by the Registrars-General of certain British Colonies, the following table has been constructed. It enables approximate comparison to be made as regards the prevalence of fatal phthisis in widely distant parts of the world. The figures indicate average crude rates of mortality from phthisis in the ten years 1893-1902 per thousand of the several populations. The countries are arranged in the descending order of their death-rates.

Austria	3·49 [1]	Scotland	1·64	Queensland	0·91
Germany	2·13	Jamaica	1·60	South Australia	0·91
Ireland	2·13	Belgium	1·41	Ceylon	0·87
Norway	1·96	England	1·34	New South Wales	0·82
Switzerland	1·92	Italy	1·24	New Zealand	0·79
Netherlands	1·65	Victoria	1·23	Tasmania	0·73
		Western Australia	0·69		

Among these countries there are twelve that have furnished, in addition to the above information, the means of calculating rates of phthisis mortality for the year 1903, and in all but three of these cases the rates for that year show a reduction on the decennial rates here given.

Tuberculous Meningitis.—As will be seen by reference to the first table in this section, the mortality from tuberculous meningitis is mainly confined to infancy and early childhood, by far the greater number of the fatal cases occurring within the first two years of life. Unlike tuberculous peritonitis, this disease is especially destructive to infants between the ages of six and twelve months. In order to trace the changes in English mortality from tuberculous meningitis, in two periods half a century apart, the following table has been constructed, giving average rates of mortality in a hundred thousand living, at all ages, and at two groups of ages.

	All Ages.		Under 5 Years.		5 to 10 Years.	
	Males.	Females.	Males.	Females.	Males.	Females.
1851-60	41	29	292	216	40	33
1901-3	20	17	117	104	29	26

Comparison of the rates of 1851-60 with those of 1901-3 shows that in the more recent period a considerable reduction has taken place in the mortality from this disease among children of both sexes under five years old. The fall has been steadily progressive throughout the

[1] Average for nine years 1893-1901.

53 years. Had this table been extended to later age-groups, it would have appeared that no corresponding reduction had occurred among adults: at the higher ages, however, the mortality becomes insignificant, and for this reason the rates are omitted from the table. It is probable that many of the deaths now referred to tuberculous meningitis would, in earlier years, have been returned as from so-called simple meningitis, or from hydrocephalus. On the other hand, it is certain that many deaths are now certified as from general tuberculosis, which, if inquiry were possible, would be relegated to the cerebral form of the disease, for which there is now a separate line in the tables.

Tuberculous Peritonitis, Tabes Mesenterica.—Under the objectionable though time-honoured name, *tabes mesenterica*, there are still commonly included, in addition to tuberculous affections of the mesenteric and retroperitoneal glands, various indefinite conditions in which intestinal irritation and general wasting are prominent symptoms. With the object of ascertaining how far the use of this term to describe the present form of tuberculosis has the sanction of the medical profession, I have recently communicated with the medical authorities of the principal hospitals in the metropolis asking for definite information on this point. Without exception, the replies are to the effect that the use of the term Tabes mesenterica has been discarded by the medical staffs of the institutions referred to. It is satisfactory to note that practitioners of medicine throughout the country are tending to follow the example of their colleagues in the public hospitals, for recent death-returns show that the term tuberculous peritonitis is rapidly displacing the objectionable name in question, which will probably soon become obsolete.

Like tuberculous meningitis, this disease is fatal mainly in childhood. The mortality among infants under one year is very high, amounting in the year 1903 to 2·66 per thousand births, the greater part of which falls on infants of from three to six months. In the second year the mortality is still excessive, but it is then less than half as high as in the first year of life. In the third and succeeding years it rapidly diminishes. Male infants in their first year suffer more severely than females in the ratio of about five to four. The rates of mortality for both sexes, at all ages and at the age-group 0-5 years, show *successive increments* from 1851-60 to 1871-80, and *successive decrements* in the subsequent decennia.

In the following table, which relates to the 33 years ended with 1903, the rates of mortality from this disease are shown per 100,000 persons living, at all ages, and at two age-groups.

	All Ages.	Under 5.	5-10.
1871-80	29	204	13
1881-90	26	181	12
1891-1900	22	146	10
1901-3	17	111	10

We thus see that among children up to the tenth year there has been a steady decrease in the mortality ever since 1871-80. The death-rates at subsequent ages are inconsiderable, but they do not indicate a similar fall.

Malignant Disease.—In the decennium ended with 1903 the deaths from cancer in England and Wales averaged 25,502 annually, and corresponded to a rate of 802 per million persons living, without distinction of age or of sex. Onwards from the earliest period regarding which official statistics exist, the record of cancer in this country is an unbroken one of steadily increasing fatality: this may be seen from the appended table, which traces that increase through four successive decennia. In 1854, the opening year of the last half-century, cancer was fatal among males at the rate of 196 per million living at all ages, and among females at the rate of 449 per million; whilst in 1903, the closing year of that period, the rates were respectively 732 and 1003 per million. In other words, the male rate of death from cancer has more than trebled within the half-century, and the female rate has more than doubled.

The variations of cancer mortality, and also its relative increase at the several stages of life, will be seen in the subjoined table, which gives for each decade of the last forty years the average rates of mortality per million of the male and female population, respectively, at the ages specified.

Ages.	Males.				Females.			
	1861-70.	1871-80.	1881-90.	1891-1900.	1861-70.	1871-80.	1881-90.	1891-1900.
All ages	240	313	437	600	532	632	756	906
0-5	13	13	21	33	13	12	19	28
5-10	8	7	11	18	7	7	9	14
10-15	7	8	12	19	7	7	10	14
15-20	18	16	23	32	16	14	18	27
20-25	26	27	37	51	32	27	33	39
25-35	60	71	80	99	161	174	173	175
35-45	205	240	299	384	670	793	855	891
45-55	539	706	1002	1300	1539	1764	2051	2323
55-65	1206	1593	2302	3160	2302	2765	3375	4099
65-75	1874	2605	3758	5325	2806	3524	4531	5829
75 and upwards	2269	2989	3926	5824	2798	3520	4601	6377

From those columns of the foregoing table which relate to the recently completed decennium, it may be gathered that cancer does not cause excessive loss of life until somewhere between the ages of 25 and 35 years—the mortality under 35 ranging, in males, from 18 per million at age 5-10, to 99 per million at age 25-35, and in females from 14 per million at age 5-15, to 175 per million at age 25-35. But from the thirty-fifth year onwards to the close of life cancer appears in the death-registers in large and steadily increasing proportions. The table further indicates that throughout the last forty years there has been a

serious and progressive increase in cancer fatality at each successive stage of life. Although at the several age-groups under 35 the rates of mortality are still small, they nevertheless show in each case a decided increase since 1861-70. From the thirty-fifth year onwards cancer fatality has increased in men much more rapidly than in women. In each successive decade of life, the increase has been progressively greater in men up to the seventy-fifth year, and in women progressively greater up to the close of life.

In the following table, which relates to the quinquennium 1899-1903, the English counties have been grouped as before, so as to show the variations of cancer mortality in town and country, in that portion of a standard million living above the age of 35 years.

	Males.		Females.		Both Sexes.	
	Crude Rates.	Corrected Rates.	Crude Rates.	Corrected Rates.	Crude Rates.	Corrected Rates.
Urban counties .	2061	2215	2892	3023	2497	2641
Rural counties .	2345	1978	3021	2674	2705	2345
England and Wales	2128	2125	2903	2901	2537	2534

The necessity of correcting rates of mortality for sex and age differences of population is forcibly illustrated in the case of cancer. This table shows that if the mortality had been measured by the uncorrected or "crude" rates, the rural counties would have appeared to suffer more severely than the urban; whereas, after making due allowances for differing constitution of the living, the position is reversed, for the mortality in the rural districts is now seen to be the lower by nearly 10 per cent.

But for communities thus variously constituted even this method of correction fails to express the true relation between the cancer mortality of the town and that of the country. A further serious and practically irremediable complication arises from the fact that many country patients die in urban hospitals. Moreover, it would obviously be rash to assume that the place of a cancer patient's residence immediately before death had been the place of origin of his or her disease.

In the three years 1901-3 the deaths from malignant disease of 33,788 males and 50,660 females, together 84,448 persons, at all ages, were registered in England and Wales. Malignant disease affects the sexes very unequally: among males cancer mortality was equal to a rate of 706 per million living of that sex, and among females, to a rate of 991 per million. The excessive recorded mortality in females depends on the tendency of cancer to invade with exceptional frequency the generative and mammary organs of that sex. Excluding affections of these organs, cancer is relatively most fatal to the male sex. This will appear from the appended table, which gives, for the period last mentioned, the

annual rate of mortality per million living, at all ages, from malignant affections of the several parts or organs of the body.

Parts affected.	Deaths.		Annual Death-rates.	
	Male.	Female.	Male.	Female.
Stomach and Œsophagus	9,456	7,844	198	153
Rectum	3,450	2,939	72	57
Other parts of the Intestines	2,385	3,338	50	65
Uterus	...	11,714	...	229
Ovary	...	920	...	18
Breast	...	8,367	...	164
Mouth, Tongue	3,210	588	67	11
Skin (Head and Face)	1,390	637	29	12
Liver and Pancreas	5,122	7,409	107	145
Bladder	1,361	483	28	9
Jaw and other Bones	1,954	1,421	41	28
Other parts	5,460	5,000	114	100
Total	33,788	50,660	706	991

Thus, in equal numbers of the living at all ages, males succumb more often than females to cancerous affections of those organs that are common to the sexes, except the liver, pancreas, breast, and intestines other than the rectum. The organs here excepted are most frequently the seat of malignant invasion in the female sex.

The following table shows, by a different method, the relative frequency with which the various organs or parts of the body are affected by malignant disease :—

MALES.

Parts affected.	Under 25.	25-	35-	45-	55-	65-	75-	85-	All Ages.
Stomach and Œsophagus	0	4	19	56	93	80	27	1	280
Rectum	1	3	6	18	31	30	12	1	102
Other parts of the Intestines	1	2	5	12	21	21	8	1	71
Mouth, Tongue	1	1	7	22	33	23	8	1	96
Skin of Head and Face	0	1	2	5	8	12	11	3	42
Liver and Pancreas	1	2	10	28	48	44	16	1	150
Bladder	0	0	1	6	10	15	7	1	40
Jaw and other Bones	5	2	5	10	15	13	7	1	58
Other parts	12	8	16	34	44	34	12	1	161
Total	21	23	71	191	303	272	108	11	1000

FEMALES.

Parts affected.	Under 25.	25-	35-	45-	55-	65-	75-	85-	All Ages.
Stomach and Œsophagus	0	3	11	28	45	48	18	2	155
Rectum	0	2	5	11	16	16	7	1	58
Other parts of the Intestines	0	1	4	12	19	20	9	1	66
Uterus	0	10	41	70	60	37	12	1	231
Ovary	1	1	3	6	4	2	1	0	18
Breast	0	3	20	42	44	33	19	4	165
Mouth, Tongue	0	1	1	2	3	4	1	0	12
Skin of Head and Face	0	0	1	1	2	4	4	1	13
Liver and Pancreas	1	2	9	25	46	44	18	2	147
Bladder	0	0	1	1	2	3	2	0	9
Jaw and other Bones	3	1	3	4	6	6	4	1	28
Other parts	6	4	10	20	25	23	9	1	98
Total	11	28	109	222	272	240	104	14	1000

The table may be read as follows:—Among males, out of every thousand fatal cases of cancer, the stomach was the organ affected in 280 cases, 4 of which occurred at ages 25 to 35, 19 at ages 35 to 45, and 93 at ages 55 to 65. . . . Again, among females, out of every thousand fatal cases of cancer, the uterus was the organ attacked in 231 cases, of which 10 occurred at ages 25 to 35, 41 at ages 35 to 45, 70 at ages 45 to 55, and so on.

We have seen that the loss of life due to malignant disease is limited mainly to ages above 35 years; it therefore follows that the mortality in any particular area will largely depend on the proportion of those living under and over middle age. The prevalence of cancer in any two places cannot safely be compared by a mere statement of their respective rates of mortality *at all ages*, unless the age and sex constitution of both populations has been ascertained to be similar. This will readily appear from the following example. In the years 1881-90 the uncorrected English rates of cancer mortality at all ages ranged from 440 per million in the county of Durham, 475 in Stafford, 477 in Lancaster, 482 in Derby and in Monmouth, and 501 in South Wales, to 716 in Norfolk, 727 in Sussex, 736 in North Wales, 740 in Devon, 789 in Cambridge, and 916 in Huntingdon. If, on the other hand, the incidence of cancer mortality be examined in that portion of a standard million living above the age of 35 years, it will be found that the highest cancer rate of all occurs in London, and that Huntingdon, Cambridge, Sussex, and North Wales are still among the counties with the highest cancer rates. But by making due allowance for age and sex differences in the living, the counties of Devon and Norfolk are removed from among the areas of excessive cancer mortality to a position below the mean for the country generally. Again, of the six counties whose uncorrected rates are below the average, there are only two, Monmouth and Derby, that, after correction, retain their former position—the places of Stafford, Lancaster,

Durham, and South Wales being taken by Dorset, Buckingham, Wilts, and Cornwall. Moreover, from what has been said, it may readily be calculated that the uncorrected rate at all ages in Huntingdon is to that in Durham as 208 to 100, but if the aforesaid correction be effected, the ratio will stand as 127 only to 100. Again, although the uncorrected rates for London and Cornwall are practically identical, the corrected rate for London is to that of Cornwall in the proportion of 138 to 100.

In the course of the inquiry into industrial mortality previously referred to, I found that among men of all occupations between the ages of 25 and 65 the comparative mortality figure for cancer in England and Wales was 44. In the industrial districts it was 48, and in London 59. It is, however, necessary to bear in mind that inasmuch as important hospitals are for the most part situated in large towns, a considerable number of country patients would probably go to those institutions for treatment, and their deaths would be registered as occurring there, thus unduly increasing the recorded cancer mortality of London and other industrial centres. The indefinite class of workers styled "artisans" appear to suffer least severely from cancer, their comparative mortality figure being only 9. Among coal-miners the cancer-mortality figure varied from 26 in Monmouthshire and South Wales to 37 in Staffordshire. At the other end of the scale, the figure was 70 for brewers, 73 for workers in tallow and glue, and 86 for copper-miners, whilst it amounted to not less than 156 for chimney-sweeps. Although these last workers still suffer terribly from this disease, there has happily been among them a great abatement of fatality since the previous record. In 1880-82 the comparative mortality figure for cancer among chimney-sweeps had been 290, whereas in 1890-92 the figure, modified for purposes of comparison, was 157, showing a reduction of little less than half.

The appended table shows the distribution of cancer mortality in various parts of the world. Returns for the ten years 1893-1902 are available from several separate countries, and from these the crude rates have been calculated per 1000 of the several populations.

Switzerland	1·26	Austria	0·67 [1]	New South Wales	0·52
The Netherlands	0·90	New Zealand	0·59	Italy	0·50
Norway	0·83	Ceylon	0·59	Queensland	0·44
England	0·79	Prussia	0·57	Hungary	0·33 [2]
Scotland	0·76	Ireland	0·57	Western Australia	0·33
Germany	0·70	South Australia	0·56	Jamaica	0·15
Victoria	0·68	Tasmania	0·55		

Of the above-named countries thirteen have furnished returns for 1903, and in all cases save one the cancer mortality in that year exceeded the average.

Diphtheria, Croup.—In the earlier years of civil registration English statistics concerning diphtheria were very unreliable, the disease having been confused with scarlet fever, and with several other conditions, *e.g.* croup, laryngitis, and quinsy. The mortality from diphtheria was not

[1] Average for 9 years 1893-1901. [2] Average for 6 years 1897-1902.

separately abstracted in the national records until 1855, in which year it was for the first time distinguished from scarlet fever; and for some years after that date the returns show curious relations between the deaths referred to diphtheria and those referred to the other conditions here mentioned. It is significant, in this connexion, that in proportion as medical diagnosis has become more exact, the mortality from so-called "croup" has fallen, whilst the mortality definitely ascribed to diphtheria has risen. This is shown by the following table, which gives the mortality per million of the population at all ages and at two age-groups (1) from diphtheria and croup separately, and (2) from diphtheria and croup together. There is little doubt that the third column of rates in this table furnishes a truer measure than does the first of the behaviour of fatal diphtheria in the last thirty years.

	All Ages.		Diphtheria and Croup.		
	Diphtheria.	Croup.	All Ages.	Under 5 Years.	5 to 10 Years.
1871-80	112	149	261	1525	503
1881-90	153	133	286	1595	641
1891-1900	263	51	314	1719	756

We thus see that throughout the last three decennia there has been in England a notable increase in diphtheria mortality—an increase affecting children more especially. In this respect diphtheria contrasts markedly with scarlet fever—the mortality from which has declined within the same period, in a degree which is very remarkable. The following table, which relates to the quinquennium ended with 1903, shows the varying incidence of mortality from diphtheria and croup in town and country. The figures represent average annual rates per thousand children living under five years, at which age diphtheria is more fatal than at other stages of life.

	Urban Counties.	Rural Counties.
Boys . .	1·86	0·96
Girls . .	1·79	0·92
Both sexes .	1·83	0·94

These figures indicate that in recent years the mortality from diphtheria has been much greater in the town than in the country—a distribution which is the opposite of that obtaining in the earlier years of civil registration, when diphtheria was commonly considered to be mainly a disease of the country. It is more than likely that the present excessive fatality of this disease as well as of most other infectious diseases, in the urban areas, is caused by the closer aggregation of school children which obtains there, as compared with the rural districts.

The following table gives, for the administrative county of London

the number and proportion of notified cases of diphtheria in the ten-year period ended with 1903, together with the percentage fatality among the attacks at the several ages. These numbers do not include cases of "croup," but as the mortality from that condition in London does not now exceed 3 per cent of that from diphtheria, the proportions in the table may be accepted with confidence.

Ages.	Cases notified.		Deaths.		Case Rate per 1000 Living.		Percentage Fatality.	
	Males.	Females.	Males.	Females.	Males.	Females.	Males.	Females.
All ages	53,671	63,890	9,059	9,592	2·5	2·8	16·9	15·0
Under 1 year	1,477	1,128	630	528	2·8	2·2	42·7	46·8
1-2	4,044	3,561	1,571	1,445	8·4	7·4	38·8	40·6
2-3	5,219	4,777	1,537	1,488	11·3	10·4	29·5	31·2
3-4	6,264	6,144	1,481	1,469	13·9	13·7	23·6	23·9
4-5	6,180	6,473	1,188	1,326	14·0	14·7	19·2	20·5
5-10	16,854	20,328	2,110	2,692	8·1	9·7	12·5	13·2
10-15	5,865	7,753	309	341	2·9	3·8	5·3	4·4
15-20	2,766	3,812	73	81	1·4	1·7	2·6	2·1
20-25	1,802	3,193	43	39	0·8	1·2	2·4	1·2
25-35	2,099	4,287	43	77	0·6	1·0	2·0	1·8
35-45	739	1,587	32	43	0·3	0·5	4·3	2·7
45-55	235	603	24	23	0·1	0·3	10·2	3·8
Above 55	127	244	18	40	0·1	0·1	14·2	16·4

This table indicates that, according to London experience, which extends to 117,561 cases within a period of ten years, the incidence of diphtheria is mainly limited to the period of childhood, the ages from two years to five being those most liable to attack. Comparatively few cases occur in the first year of life, but the fatality among infants attacked at that age is excessively high. In proportion to population the notified cases are comparatively few in number after the tenth year of life, and the case fatality is below the mean except among women above the age of 55 years.

The following table shows the daily average of diphtheria attacks in London in each month of the fourteen years ended with 1903:—

	Daily Average.		Daily Average.		Daily Average.
January . .	27·2	May . . .	27·0	September . .	33·3
February . .	27·5	June . . .	27·9	October . .	39·0
March . .	25·0	July . . .	32·1	November .	36·3
April . .	23·4	August . .	28·0	December . .	31·7

November and October would thus appear to be the periods of greatest diphtheria prevalence in London, the daily average of attacks in these months being 36 and 39 respectively; and April would appear

to be the month of least prevalence, the daily average being only 23, as against a daily average of 30 for the entire year.

The following table, which relates to the decennium ended with 1902, shows the mortality from diphtheria in various parts of the world. The figures denote average crude rates per million of the several populations.

Prussia .	. *783	Italy .	. *294	Victoria .	. 137	New Zealand	94
German Emp.	*671	England .	. 274	N.S. Wales	. 136	West Australia	88
Sweden .	. *500	Norway .	. *273	Queensland	. 132	Ireland	. 81
Switzerland	. *343	Scotland .	. 178	Tasmania	. 123	Jamaica	. 15
Belgium .	. *326	S. Australia	. *158	Netherlands	. 122	Ceylon	. *8

In the countries marked with an asterisk the numbers include deaths from "croup" as well as from diphtheria.

Enteric Fever.—Not until the year 1869 was this disease distinguished, in the national records, from other forms of continued fever; consequently, for periods anterior to that date no reliable statistics exist concerning the fatality of enteric fever in this country. In the five years 1869-73 the deaths from enteric fever in England and Wales averaged 8677 annually, and were in the proportion of 380 per million living at all ages, without regard to sex. In the five years ended with 1903 the annual average number was 4892, and the rate of mortality only 150 per million—a reduction equal to 61 per cent within a period of thirty-five years.

In order to illustrate the changes in the age and sex distribution of fatal enteric fever since 1871-80, the following table has been prepared—the figures denote corrected rates of mortality for each sex per million of the population at the several groups of ages :—

Ages.	Males.			Females.		
	1871-80.	1881-90.	1891-1900.	1871-80.	1881-90.	1891-1900.
All ages	325	214	200	319	183	150
0-5	398	131	85	405	128	80
5-10	309	170	120	366	189	134
10-15	274	192	152	352	226	172
15-20	377	300	279	438	281	233
20-25	432	338	347	336	234	205
25-35	311	273	296	280	197	186
35-45	259	202	227	239	165	154
45-55	273	177	174	230	136	117
55-65	291	166	137	248	122	90
65-75	341	132	87	256	99	54
75 and upwards	259	71	36	187	55	24

From this table it appears that the sex incidence of fatal enteric fever has altered considerably in the course of the last thirty years. In the first decennium of that period both sexes fell victims in nearly equal proportions, in the succeeding decennium the male rate considerably

exceeded the female, whilst in the latest decennium the female rate was not more than three-fourths of the male. Up to the age of fifteen years the decrease in fatality has been about equal in both sexes, but from that age up to the forty-fifth year the fall has been considerably greater among females.

The following table, which relates to the five years 1889-1903, shows the differences in enteric fever mortality in town and country. As usual, the figures denote corrected rates of mortality at all ages in each million of the respective populations.

	Males.	Females.	Both Sexes.
Urban counties . .	207	143	174
Rural counties . .	103	84	93
England and Wales .	179	123	150

From these data it will readily be gathered that the same number of persons among whom 100 deaths from enteric fever occurred in the rural group of counties, contributed 187 deaths in the urban group. The peculiarity already established with respect to phthisis is equally characteristic of the disease now in question—namely, that among males the unwholesome conditions of town life tend to greater excess of fatality than among females. The figures last given indicate this clearly. For while males are subject to a mortality from enteric fever which is greater by 101 per cent in the urban counties than in the rural, the excess among females is not more than 70 per cent.

The subjoined table gives, for the administrative county of London, the number and proportion of notified cases of enteric fever in the last ten years in each thousand of the population, together with the percentage case fatality at the several ages.

Ages.	Cases notified.		Deaths.		Case Rate per 1000 Living.		Percentage Fatality.	
	Males.	Females.	Males.	Females.	Males.	Females.	Males.	Females.
All ages	18,756	15,115	3540	2534	0·9	0·7	18·9	16·8
Under 1 year	24	23	10	11	0·0	0·0	41·7	47·8
1-2	91	65	13	13	0·2	0·1	14·3	20·0
2-3	177	138	23	23	0·4	0·3	13·0	16·7
3-4	270	262	34	23	0·6	0·6	12·6	8·8
4-5	339	296	28	33	0·8	0·7	8·3	11·1
5-10	2,231	1,989	165	172	1·1	0·9	7·4	8·6
10-15	3,011	2,327	254	248	1·5	1·1	8·5	10·7
15-20	2,971	2,216	485	360	1·5	1·0	16·3	16·2
20-25	2,729	2,201	621	370	1·2	0·8	22·9	16·8
25-35	4,003	3,180	1033	638	1·1	0·7	25·8	20·1
35-45	1,837	1,491	498	357	0·6	0·5	27·1	23·9
45-55	737	643	229	175	0·4	0·3	31·1	27·2
Above 55	336	284	144	111	0·2	0·1	42·9	39·1

It would appear from this table that the period of life intervening between the tenth year and the twentieth is exceptionally liable to attack by enteric fever, the cases at those ages being most frequent among boys. According to London experience, only a few cases occur during the first year of life, but the cases that do occur are excessively severe. At the age 20-25 the fatality of enteric fever begins to exceed the mean, and the excess increases steadily from that age onwards to the close of life.

The seasonal incidence of enteric fever is shown by the following table, which is based on 46,125 cases notified in London in the fourteen years ended with 1903 :—

	Daily Average.		Daily Average.		Daily Average.
January	8·1	May	5·2	September	13·1
February	6·6	June	6·3	October	15·8
March	5·5	July	7·0	November	15·7
April	4·8	August	8·7	December	11·5

As the daily attacks average nine in number for the entire year, it follows that October and November are the months of greatest prevalence, the daily attacks averaging sixteen in number; whilst April and May are the months of least prevalence, the daily average of attacks being only five.

In the subjoined table the distribution of enteric fever mortality is shown in various colonies and in certain foreign countries in the ten years ended with 1902. The figures represent average crude rates per million of the several populations.

Norway	70	New Zealand	132	Belgium	251
Switzerland	87	Sweden	151	Victoria	254
Netherlands	101	Scotland	167	South Australia	255
Jamaica	106	England	172	Queensland	275
German Empire	113	Ireland	190	New South Wales	277
Prussia	132	Tasmania	246	Italy	461

The number of deaths and the estimated populations have been derived from the countries making the returns; the rates have been calculated for the purpose of the present article.

Measles.—Although this disease is responsible for about 10,000 deaths annually in England, only limited attempts have as yet been made to bring the salutary influence of compulsory notification in its entirety to bear upon it. Within the last year, however, the London County Council has decided to apply to measles certain of the provisions (short of compulsory notification) contained in the Public Health Act. It remains to be seen to what extent the County Council's action will be effective in controlling the spread of measles in the Metropolis.

The following table shows the changes of mortality from measles in this country in the course of the last thirty years. The figures represent average rates per million living.

	All Ages.	Under 5 Years.	5 to 10 Years.
1871-80	334	2579	208
1881-90	406	3127	271
1891-1900	414	3247	221

We thus see that there has been a rise in measles fatality in the general population since the period 1871-80; indeed, among children, who are the chief sufferers from this disease, the mortality has increased considerably.

The following table, which relates to the period 1899-1903, has been prepared to show the varying incidence of measles fatality in the urban as compared with the rural districts of England. The figures denote rates of mortality per 1000 children living under five years of age.

	Urban Counties.	Rural Counties.
Boys . . .	3·58	1·31
Girls . . .	3·29	1·25
Both sexes . .	3·43	1·28

This table shows that measles, like many other infectious diseases, is much more fatal in the town than in the country, and that in both areas it levies the highest death-toll among boys. In these respects the behaviour of measles corresponds to that of several other diseases which mainly afflict infant life.

The following table shows the distribution of mortality from measles in foreign countries, as far as this has been hitherto ascertained by the English Registrar-General. The figures represent average uncorrected rates of mortality per million living at all ages in the ten years 1893-1902.

Belgium	442	German Empire .	260	Victoria . .	136	Sweden . .	96
Scotland	435	The Netherlands	230	New South Wales	135	West Australia	93
England	391	Ireland . .	182	Queensland . .	127	Ceylon . .	82
Italy .	277	South Australia .	177	New Zealand .	121	Tasmania .	67
Prussia	266	Switzerland .	154	Norway . .	101	Jamaica . .	47

As far as the United Kingdom is concerned, it is remarkable that the measles death-rate of Ireland should average less than half that of either England or Scotland.

Scarlet Fever.—In the first list of diseases issued from the General Register Office by Dr. Farr, scarlatina appears as one of the chief causes of death; but the numbers for the several years previous to 1855 included in addition the deaths from diphtheria, and it is probable that for many years subsequently the two diseases were but imperfectly differentiated in the medical certificates of cause of death.

In the following table the mortality from scarlet fever is shown at all ages, and at three age-groups, in each decennium of the last thirty years. The figures denote rates per million living at each period.

	All Ages.	Under 5 Years.	5 to 10 Years.	10 to 15 Years.
1871-80	649	3504	1522	326
1881-90	312	1667	763	154
1891-1900	158	844	353	81

In the present, as in other tables in this article, the rates have been recalculated, and corrected for age and sex differences of population. It is beyond question that in the course of the last thirty years English mortality from scarlet fever has decreased greatly and very rapidly; and, moreover, that the fall has been remarkably uniform at those ages which are particularly susceptible to infection.

The subjoined table, which relates to the quinquennium 1899-1903, is intended to show the varying incidence of fatal scarlet fever with respect to locality, in that section of the population which is most liable to fatal attack. The figures denote average annual rates of mortality in 100,000 living under five years of age.

	Urban Counties.	Rural Counties.
Boys . . .	93	32
Girls . . .	87	29
Both sexes . .	90	31

These figures show that scarlet fever causes much greater loss of life in the town than in the country.

The following table, which relates to the administrative county of London, gives the number and proportion of cases of scarlet fever notified in the decennium 1894-1903, and also the percentage fatality among the attacks at the several ages :—

Ages.	Cases notified.		Deaths.		Case Rate per 1000 Living.		Percentage Fatality.	
	Males.	Females.	Males.	Females.	Males.	Females.	Males.	Females.
All ages	88,147	96,495	3299	3103	4·2	4·3	3·7	3·2
Under 1 year	1,450	1,229	205	165	2·7	2·4	14·1	13·4
1-2	3,658	3,437	465	423	7·6	7·2	12·7	12·3
2-3	6,456	6,174	614	566	14·0	13·4	9·5	9·2
3-4	8,471	8,643	576	565	18·8	19·3	6·8	6·5
4-5	9,114	9,476	404	350	20·6	21·5	4·4	3·7
5-10	33,712	38,068	704	729	16·2	18·2	2·1	1·9
10-15	14,423	16,607	150	135	7·2	8·2	1·0	0·8
15-20	5,484	5,447	70	47	2·7	2·4	1·3	0·9
20-25	2,643	3,352	54	58	1·2	1·3	2·0	1·7
25-35	2,027	3,037	36	45	0·5	0·7	1·8	1·5
35-45	511	765	11	9	0·2	0·2	2·2	1·2
45-55	143	188	7	7	0·1	0·1	4·9	3·7
Above 55	55	72	3	4	0·0	0·0	5·5	5·6

Inasmuch as this table is based on the experience of London during ten years, under the full operation of compulsory notification, and as it relates to 184,642 cases of scarlet fever reported in that period, the proportions given may be taken as fairly representing the normal age and sex distribution of that disease, as well as its case fatality at the several ages. In relation to population both sexes appear to be about equally susceptible to infection by scarlet fever. Although the incidence of that disease is mainly confined to childhood, only comparatively few cases are recorded in the first year of life. The chief incidence of attack appears to be on the ages from two to ten years, although the fatality among the cases attacked is not then so great as it is among infants who have not attained their first birthday.

In the next table, which likewise relates to the administrative county of London, the daily average number of scarlet fever attacks is shown in each month of the period 1890-1903.

	Daily Average.		Daily Average.		Daily Average.
January	43·0	May	46·6	September	70·2
February	39·1	June	52·5	October	82·0
March	37·2	July	62·0	November	69·1
April	39·6	August	55·7	December	50·6

From this table it appears that the autumn is the season of greatest scarlet fever prevalence in the metropolis. According to the experience of the last fourteen years, the month in which the attacks are most numerous is October, the daily average in that month being 82, against a daily mean of 54 for the entire year.

With respect to the seasonal incidence of this disease, as well as of diphtheria, in London, I would refer the reader to the weighty evidence collected in the course of fourteen years by the County Medical Officer of Health. Commenting on the evidence, contained in his successive annual reports, Sir Shirley Murphy adverts to the influence of school attendance on the prevalence of both these diseases—showing that this varies widely according as the period in question corresponds to the interval of school closure for the holidays, or to the period of compulsory attendance at school.

The following table shows the distribution of scarlet fever mortality in some of our colonies and in certain foreign countries, in the ten-year period 1893-1902. The figures denote average crude rates of mortality in each million of the several populations.

Prussia	276	Italy	110	The Netherlands	32
German Empire	213	Ireland	91	South Australia	28
Belgium	189	Norway	81	Victoria	28
Scotland	170	New South Wales	52	Switzerland	20
England	151	Tasmania	38	New Zealand	12
Sweden	133	Queensland	35	Western Australia	6

In the ten years above referred to no deaths from scarlet fever were

returned from Ceylon, and only one death was reported from Jamaica. The actual deaths and the populations for this and subsequent similar tables have been derived from the contributing countries; for the calculation of the rates, I am myself responsible.

Small-pox, Chicken-pox.—Both the prevalence and the fatality of small-pox in any time or place depend absolutely on the condition of the community with respect to vaccination. That such is the case has been conclusively proved, but this point is sufficiently discussed in the special article on small-pox in the second volume of this System, to which, therefore, the reader is referred.

As compulsory notification of infectious diseases throughout the country was not provided for by legislation until the year 1899, the past history of small-pox must be gleaned almost entirely from the death-registers. In the course of the last half-century the changes of small-pox mortality in England and Wales have been as follows. In the first decennium of that period, namely, in 1851-60, small-pox accounted for a mortality of 221 per million living—a rate which fell to 152 per million in the succeeding decennium. In the ten years ended with 1880 the rate increased to 230 per million, but in the two succeeding decennia there was again a fall—the rate being 44 per million in 1881-90, and only 13 per million in 1891-1900. Inasmuch, however, as the degree of vaccinal protection possessed by the people varies enormously, not only in different communities simultaneously, but even in the same community at different times, it follows that in a population exceeding 30 millions small-pox may effect terrible havoc among certain sections of the people without seriously raising the death-rate of England and Wales as a whole. For this reason, amongst others, there is obviously a limit to the value of small-pox mortality statistics.

The experience of London with respect both to small-pox and to chicken-pox is unique. Compulsory notification was adopted here in 1889, and ever since that year the reported cases of small-pox in the metropolitan population of more than 4,000,000 have been registered weekly, the sex incidence and the mortality of the reported cases being carefully recorded for the several municipal areas (9).

With respect to two considerable periods in the course of the recent prevalence of small-pox in London similar records have been kept for chicken-pox, the County Council having scheduled that disease as temporarily notifiable under the local Act (10).

From Sir Shirley Murphy's successive reports we learn that in the course of the fourteen years ended with 1903, not fewer than 15,976 cases of small-pox and 35,883 cases of chicken-pox were notified within the administrative county. That small-pox prevalence in London is commonly the result of importation from the Continent will be seen by the remarks accompanying the reports already referred to. The volume for 1903 contains the number of small-pox attacks reported in each year since the establishment of compulsory notification. The following table is derived from official sources (11):—

1890	60	1895	980	1900	86
1891	114	1896	225	1901	1700
1892	425	1897	104	1902	7796
1893	2815	1898	33	1903	416
1894	1193	1899	29	1904	489

We thus see that in the period here referred to there have been two principal intervals of small-pox prevalence in London, the first extending over more than five years and culminating in 1893, the second and more extensive outbreak having been practically suppressed in two years, with a maximum incidence in 1902.

The mean daily incidence of attack in each month of the year may be seen from the following table, which is based on figures kindly given me by the County Medical Officer of Health :—

January	3·1	May	4·8	September	1·4
February	4·9	June	3·7	October	1·0
March	5·2	July	2·4	November	1·9
April	5·1	August	2·0	December	2·1

From this table, and from the chart on p. 12 of the 1903 report, it appears that, according to London experience in the last fourteen years, the incidence of small-pox is enormously greater in the first half than in the second half of the year. March is the month of greatest prevalence, the reported cases being then in excess of the average by from 70 to 80 per cent. In October the attack-rate is lowest, falling in the second week of that month to 75 per cent below the average. The opinion of medical officers of health is unanimous in attributing the spread of small-pox, in most instances, to exposure of unrecognised cases of that disease among the people. These cases are often mistaken for chicken-pox, and, for this reason, it may be of interest to medical practitioners to be informed of the age incidence of the cases recently reported in London as from that disease. The following table, which is derived from the County Medical Officer's returns, shows the proportion of attacks occurring at the several ages, the attacks at all ages being taken as 100. The total numbers reported were 25,000 in the year 1902, and nearly 11,000 in 1904.

	All Ages.	Under 1 year.	1-2.	2-3.	3-4.	4-5.	5-10.	10-15.	15-20.	20 and upwards.
1902	100	9·8	9·7	9·5	11·8	13·4	36·8	5·5	1·5	2·0
1904	100	10·1	11·0	10·7	11·2	12·7	34·9	6·0	1·6	1·8

Further remarks on the relation of small-pox to chicken-pox are unnecessary here, the subject having been exhaustively treated of in Sir Shirley Murphy's reports before referred to.

Whooping-cough.—This is another of those infectious diseases that year by year exact a heavy death-toll from the infantile population of this country, the annual number of deaths, mainly those of

children, attributed to this disease averaging about ten thousand. The following table shows the variations in mortality from whooping-cough in each decade of the last thirty years. The figures represent average rates per million living, at the several ages.

	All Ages.	Under 5 years.	5 to 10 years.
1871-80	451	3667	135
1881-90	414	3366	128
1891-1900	377	3086	96

From these figures it appears that there has been in recent years some slight reduction in the mortality from whooping-cough. As regards the sex incidence of this disease, there exists a constant peculiarity which will be explained presently.

The following table has been prepared in order to show the effect of locality in determining the mortality from whooping-cough. The figures denote average annual rates of mortality in the five years ended with 1903, in a thousand children living under the age of five years.

	Urban Counties.	Rural Counties.
Boys	2·69	1·97
Girls	3·24	2·22
Both sexes . . .	2·97	2·10

We thus learn that as regards loss of life from whooping-cough, dwellers in the town fare much worse than those in the country; this is probably due, as in the case of many other epidemic diseases, to the closer aggregation of susceptible children prevailing in urban districts. The peculiarity above referred to with respect to sex incidence, consists in the fact that, unlike most other infectious diseases, whooping-cough shows a constant tendency to attack girls with greater severity than boys —and this is true for infants in their first year, as well as for children under the age of five years (12).

The following table shows the distribution of whooping-cough fatality in several of our colonies and in certain foreign countries. The facts of death for the several countries have been collected by the English Registrar-General. The numbers in the table, for the calculation of which I am personally responsible, represent average crude rates of mortality at all ages, in the ten years ended with 1902, per million of the several populations.

Scotland .	510	Netherlands .	264	Norway . .	179	Victoria .	116
Belgium .	475	Ireland . .	260	Switzerland .	179	Tasmania .	113
Prussia . .	421	Italy . .	234	Queensland .	178	W. Australia	100
German Empire	380	Jamaica . .	210	S. Australia .	166	New Zealand	100
England .	347	Sweden . .	183	N.S. Wales .	164	Ceylon .	19

Pneumonia.—This is one of the diseases the mortality from which would seem by the tables to have increased considerably within the last quarter of a century. The recorded increase, however, in recent years is certainly to some extent apparent only—depending partly on changes of classification. Pneumonia is now classed among the "infections," and therefore, when several causes of death are specified in a certificate, this disease is selected for statistical purposes in preference to other conditions still designated local, such as bronchitis, laryngitis, etc. The following table, which gives the average rates of mortality in England per thousand males and females living at the several ages, shows the increase of fatality attributed to this disease in the course of the last three decennia :—

	Males.			Females.		
Ages.	1871-80.	1881-90.	1891-1900.	1871-80.	1881-90.	1891-1900.
All ages	1·13	1·25	1·47	·78	·84	1·00
0-5	4·37	4·00	5·43	3·63	3·33	4·47
5-10	·26	·30	·30	·26	·30	·29
10-15	·10	·12	·11	·11	·12	·11
15-20	·20	·24	·26	·15	·17	·16
20-25	·34	·38	·38	·19	·23	·19
25-35	·51	·64	·60	·29	·36	·31
35-45	·89	1·14	1·18	·42	·55	·55
45-55	1·27	1·69	1·80	·52	·68	·78
55-65	1·80	2·35	2·58	·93	1·25	1·40
65-75	2·45	3·24	3·55	1·63	2·09	2·45
75 and upwards	2·79	3·70	4·48	2·10	2·82	3·61

This table shows that the loss of life due to pneumonia is greatest, at the several age-groups, among males. In both sexes the mortality is much higher in children under five years, and in adults above seventy-five, than in persons at intervening ages. We note further that the increase in mortality from pneumonia affects all ages and both sexes. This disease is much more destructive to life in the town than in the country, in which respect it closely resembles enteric fever [*q.v.*]. The local distribution of fatal pneumonia in the urban and rural counties of England is shown in the following table, which relates to the quinquennial period ended with 1903 ; the numbers represent average rates per thousand living at all ages :—

	Males.	Females.	Both Sexes.
Urban counties . . .	1·84	1·27	1·54
Rural counties . . .	·98	·68	·82
England and Wales . .	1·52	1·05	1·28

It may readily be calculated from the data here given that the same number of persons among whom 100 deaths from pneumonia have

occurred in the rural group of counties, have lost by death no fewer than 188 in the urban group.

In the following table, which relates to English industrial mortality in 1890-92, the incidence of fatal pneumonia in several occupations is compared with that of "farmers"—the rate of mortality from that disease in the latter being taken as 100 :—

	Farmers . 100		
Coal-heavers . . .	498	Lace manufacturers . .	96
Dock-labourers . .	440	Gardeners	94
Cutlers	410	Clergymen . . .	90
File-makers . . .	394	Schoolmasters . . .	86

From this it appears that pneumonia causes, amongst coal-heavers, dock labourers, and cutlers, a mortality more than four times, and among file-makers a mortality nearly four times as great as the standard rate for farmers; whilst the mortality in the remaining occupations in the list is below that standard.

Influenza.—An instructive and a vivid account of the havoc that, in the early days of civil registration, influenza could wreak on an over-crowded, under-fed, and ill-housed population will be found in Dr. Farr's "Tenth Report to the Registrar-General." The passage does not lend itself readily to condensation, and therefore the reader must refer to the original.

From the year 1853 until the onset of the epidemic of 1890, an interval of more than thirty years, there had been in this country no serious epidemic of influenza, although a certain number of deaths are always referred to this disease even in non-epidemic years. The epidemic which became seriously fatal in 1890 really began towards the close of the previous year, the disease having been probably imported from abroad. The statistics of influenza mortality are extremely unsatisfactory, a large but unfortunately very inconstant proportion of the deaths presumably caused by this disease being returned in the certificates, not under influenza, but under such diseases as pneumonia and bronchitis.

When influenza is unusually prevalent, especially at the beginning of an epidemic, the reported mortality from the diseases last mentioned increases rapidly. As regards pneumonia, this was especially noticeable in 1890, when without assignable cause other than the simultaneous presence of influenza the mortality from pneumonia rose to 40 per cent above the normal. In a commentary on influenza prevalence contained in his report for 1891, my predecessor, Dr. W. Ogle, gave reasons for doubting whether the influenza deaths of ordinary years are of the same nature and due to the same cause as are the deaths in epidemic periods. Considerable further experience of this malady induces me to agree with Dr. Ogle in this particular. In some parts of the country the deaths first referred to would be returned as from pneumonia or bronchitis; in others, as from influenza.

In the following table the rate of mortality from influenza is shown for each of the fourteen years since the onset of the epidemic, which even

yet cannot be said to have terminated. The figures represent annual crude rates of mortality at all ages per million living of each sex.

Year.	Males.	Females.	Year.	Males.	Females.
1890	173	142	1897	205	187
1891	612	538	1898	329	332
1892	537	530	1899	395	385
1893	334	317	1900	493	514
1894	222	218	1901	185	163
1895	419	427	1902	228	218
1896	128	116	1903	190	189

It will thus be seen that, if the figures are to be trusted, this country has never been free from fatal influenza since the beginning of the epidemic in 1890 ; and further, that subsequent to the apparent subsidence of the epidemic in 1894, at least two recrudescences have occurred, namely, in 1895 and in 1898-1900. In order to indicate the changes that have taken place since 1847-48 in the age incidence of fatal influenza, I have arranged the figures in the second column of the subjoined table in contrast with those in the first column, which were calculated by Dr. Ogle. The figures in both cases represent rates of mortality per million living at the several age-groups (13).

Ages.	1847-48.	1890-1903.
Under 5 years	713	251
5-10	80	43
10-15	49	36
15-25	51	84
25-35	79	137
35-45	139	244
45-55	284	424
55-65	809	861
65-75	2,372	1891
75-85	5,510	3674
85 and upwards	11,243	6171

A considerable change seems to have taken place in the age distribution of this disease, the rates in 1890-1903 having increased notably in the later period at ages from 15 to 65, whilst at more advanced ages they have very greatly decreased.

Rheumatic Fever.—Since the recognition in this country of the infective nature of rheumatic fever or acute rheumatism, much interest has been aroused in regard to the causes and fatality of this disease. Only since the beginning of the current century has rheumatic fever been abstracted separately from rheumatism of the heart, in the English death returns. Before 1901 the two lines were amalgamated, consequently,

with respect to the former disease alone, comparison of the present with the past is impracticable. In the course of the last three years, however, 6128 deaths have been medically certified as from rheumatic fever (including sub-acute as well as acute rheumatism), a number perhaps sufficient to justify the calculation of the death-rates hereto appended :—

Annual Death-rate from Rheumatic Fever, 1901-1903.

	All Ages.	Under 5.	5-10.	10-15.	15-20.	20-25.	25-35.	35-45.	45-55.	55-65.	65 and upwards.
Males .	64	17	59	82	82	54	70	78	75	69	54
Females .	60	18	69	90	83	57	51	58	68	56	56

It thus appears that, according to recent English experience, females are more liable than males to die of this disease up to the age of 25 years, whilst after that age the reverse is generally the case. The fatality of rheumatic fever is highest in both sexes from the tenth to the twentieth year, and lowest at ages under five. In preparing the second volume of my supplement to the Registrar-General's Fifty-fifth Report, I found that, in the three years 1890-92, the comparative mortality figures for rheumatic fever and rheumatism of the heart taken together were as follows, the mortality among all occupied males being taken as 100, for comparative purposes :—

Occupied males . . . 100

Innkeepers (London)	400	Clergymen	157
Copper-miners	400	Seamen	57
Bookbinders	214	Physicians	43
Wool manufacturers	200	Shoemakers	43
Brewers	186	Locksmiths	43
Slaters	171	Shipwrights	43
Cotton manufacturers	171	Labourers (London)	43

It must be remembered, however, that in addition to the deaths from rheumatic fever, the figures in this list include those referred to heart disease the result of rheumatism.

Diabetes Mellitus.—This disease, which is here distinguished from the condition known as diabetes insipidus, destroys on the average 2800 persons annually in England and Wales. In childhood the mortality from this disease is inconsiderable, but at ages after middle life it becomes serious. In the course of the last thirty years the mortality from diabetes mellitus has steadily increased, especially at the higher ages. This will be seen by the following table, which gives the average rate at specified ages per million of the population of each sex :—

		All Ages.	10-15.	15-20.	20-25.	25-35.	35-45.	45-55.	55-65.	65-75.	75 and upwards.
1871-1880	Males	51	10	24	34	48	69	96	182	248	172
1881-1890	Males	71	14	26	35	59	79	135	282	399	315
1891-1900	Males	86	16	32	43	57	87	161	347	559	474
1871-1880	Females	28	10	14	18	27	35	50	88	107	68
1881-1890	Females	46	15	22	27	36	51	82	161	208	181
1891-1900	Females	66	17	25	31	42	56	112	258	380	312
1871-1880	Both sexes	39	10	19	25	37	51	72	132	172	113
1881-1890	Both sexes	58	15	24	31	47	64	107	218	294	239
1891-1900	Both sexes	75	17	29	36	49	71	136	300	460	380

If the figures for the decennium last completed be examined, it will be found that the incidence of mortality from diabetes mellitus is mainly upon the ages above 35 years, the excess at the ages from 55 to 75 being especially noteworthy. At these ages the disease has been much more fatal to men than to women throughout the thirty years included in the table. Nevertheless it is among women that the fatality of the disease is increasing most rapidly.

Diabetes mellitus is one of the diseases the industrial distribution of which among males aged from 25 to 65 years was ascertained by myself after the census of 1891. The following table shows the mortality in several of the occupations dealt with on that occasion, the rates of mortality for each being compared with that of all occupied males, the latter taken as 100:—

Occupied males . . 100

Lawyers	400	Commercial travellers	186
Medical men	314	Tanners	43
Innkeepers	271	Copper-workers	43
Clergymen	243	Locksmiths	43
Brewers	243	Coal-miners (Derby)	43
Lead-miners	214	Stone-quarriers	43
Railway engine-drivers	200	General labourers	43

In the learned professions the mortality from diabetes mellitus is excessively high, and so also is it among brewers and innkeepers. It is interesting to note that among labourers, stone-quarriers, and Derbyshire coal-miners, as well as among those employed in the three other bracketed industries, the mortality from diabetes is less than half that among other occupations.

Syphilis.—If the mortality ascribed to syphilis in the last three years be compared with that in an equal period a quarter of a century ago, a reduction will be seen to have taken place at all ages equal to 35 per cent among males, and to 43 per cent among females. The returns under this heading are very far from complete, and for obvious reasons the mortality from this cause is much understated. The following table shows the age distribution of the recorded mortality from syphilis in England and Wales during the three years ended with 1903:—

	All Ages.	0-5.	5-15.	15-25.	25-35.	35-45.	45-55.	55-65.	65 and upwards.
Males . .	60	368	2	4	26	35	40	39	27
Females .	46	304	2	5	18	27	29	23	15
Both sexes .	53	337	2	4	22	31	34	31	20

From this it appears that in proportion to population syphilis now destroys more males than females, and the same disparity was observed twenty-five years ago. The table shows that the actual loss of life is by far the greatest in childhood, but unfortunately the after-effects of this infection are not adequately shown in the published returns.

General Paralysis of the Insane.—To those who are specially interested in the treatment of insanity the reason for inserting, in this order, statistics concerning general paralysis will be apparent. In the national registers the mortality from this disease was not differentiated from that due to other forms of mental disease until the year 1901. The figures in the following table represent average rates of mortality at the several age-groups in the three years 1901-3 :—

	All Ages.	0-5.	5-15.	15-25.	25-35.	35-45.	45-55.	55-65.	65 and upwards.
Males . .	104	...	1	7	79	307	298	254	273
Females .	33	...	1	5	24	69	86	76	135
Both sexes .	67	...	1	6	50	184	188	159	195

What is particularly striking in this table is the enormous excess of mortality from general paralysis which attaches to the male sex, not at all ages only, but at every stage of adult life. Although the general mortality does not bulk largely in the death-returns, the table shows that shortly after the age of puberty men fall victims to this disease in very large proportions. Statistics concerning mortality from general paralysis are perhaps more reliable than those relating to many other diseases, from the fact that most of the deaths take place in lunatic asylums, where the certificates are signed by practitioners specially experienced in the treatment of this disease.

Acute Nephritis, Chronic Nephritis, Bright's Disease.—It is perhaps difficult to justify on scientific grounds the grouping under the same head of such diseases as those returned under the above designations. But, on the other hand, it might be contended that a group of maladies destroying annually some 12,000 persons is worthy of consideration in a statistical essay. For many years past the attempt has been made, though perhaps with imperfect success, to distinguish the acute cases of nephritis from those forms variously described as chronic nephritis, Bright's disease, or albuminuria. In these circumstances it has been decided to include a brief statistical notice of this group, in the hope that it may prove serviceable to those who are without ready access to the official records.

In the course of the last 35 years Bright's disease, acute as well as chronic, has steadily increased in fatality. Taking all forms together, the death-rate at all ages, which in 1866-70 had not exceeded 106 per million of both sexes, was equal to 278 per million in the five years ended with 1900.

The following table, which refers to the three years 1901-3, gives the average rates of mortality from this group of diseases at the several ages, distinguishing males from females :—

	All ages.	0-5.	5-15.	15-25.	25-35.	35-45.	45-55.	55-65.	65 and upwards.
Males . .	423	170	60	81	172	385	868	1762	2884
Females .	334	133	55	80	176	371	623	1121	1834
Both sexes .	377	151	57	80	174	378	741	1417	2291

It is not until the mortality from these conditions is analysed according to age as well as to sex, that its true importance can be appreciated. The above table shows that although at the earlier ages the mortality thus caused is not excessive, it becomes very serious at the later stages of life, amounting to 2884 per million men, and to 1834 per million women, in the aggregate population of England and Wales.

Infantile Mortality.—If justification were needed for the inclusion in the present article of a section on infantile mortality, this may be found in the somewhat disquieting fact that although at all other stages of life English mortality has very considerably declined in the last quarter of a century, the mortality of infants has remained stationary; indeed, in the more populous districts it has actually increased. From a preventive point of view, infantile mortality is specially important, for it is universally regarded as the most reliable test of the health of communities.

For the information of the Duke of Devonshire's Committee of last year on Physical Deterioration, on which Committee I had the honour to serve, I prepared a statistical review of English infantile mortality in the last quarter of the nineteenth century—an undertaking which, involving as it did the abstraction and classification of a million deaths and of a much greater number of births, caused the expenditure of much time and of considerable clerical labour. It should here be mentioned that in consequence of the unreliability of estimates of population at the earliest ages, the rates of mortality here given are calculated—not on the numbers supposed to be living at ages under one year, but on the births actually registered in the specified periods. For the purposes of my review, the English counties were grouped in the manner already explained; the object being to contrast the mortality of the country with that of the town, in two periods a quarter of a century apart. For each of these groups infantile mortality from several causes was calculated, as in the appended table (*a*) for the quinquennium 1873-77, and (*b*) for the quinquennium 1898-1902 (14).

Infantile Mortality—Deaths under 1 Year per 1000 Births.

Causes of Death.	Urban Counties.				Rural Counties.			
	Boys.		Girls.		Boys.		Girls.	
	1873-1877.	1898-1902.	1873-1877.	1898-1902.	1873-1877.	1898-1902.	1873-1877.	1898-1902.
All causes . . .	176	180	146	149	140	139	113	111
Small-pox . . .	·5	...	·5	...	·1	...	·1	...
Measles . . .	3·0	3·7	2·6	3·2	1·6	1·8	1·3	1·6
Scarlet fever . . .	1·5	·3	1·3	·2	1·1	·1	·8	·1
Diphtheria and croup .	1·2	·8	·9	·6	·9	·4	·7	·3
Whooping-cough . .	5·9	5·2	6·6	5·8	5·0	5·3	5·1	5·6
Erysipelas . . .	·9	·3	1·0	·4	·7	·2	·6	·2
Diarrhœal diseases .	22·1	36·6	18·8	32·5	11·1	18·5	9·3	14·8
Syphilis . . .	2·2	1·5	2·0	1·3	1·1	·8	·9	·7
Rickets	·1	·8	·1	·5	·1	·5	...	·4
Tuberculous diseases .	11·8	8·2	9·3	6·6	7·9	5·2	6·4	4·2
Convulsive diseases .	32·0	23·3	24·5	18·2	26·3	20·1	19·8	15·2
Bronchitis, laryngitis .	20·6	16·5	16·3	13·4	12·7	12·7	9·8	10·2
Pneumonia . . .	9·8	13·8	7·6	10·8	7·2	9·4	5·2	6·9
Premature birth . .	14·2	22·3	11·6	17·9	12·6	20·7	10·0	16·7
Congenital defects .	2·0	5·3	1·8	4·1	1·9	4·6	1·7	3·7
Teething . . .	3·6	2·8	2·9	2·3	2·4	2·0	1·7	1·7
Atrophy . . .	29·9	23·8	25·8	19·4	33·0	23·7	27·5	18·8

The most remarkable feature in this table is the comparatively small variation in the infantile mortality from all causes that has occurred in the course of 25 years—the change in the urban counties being an increase of between two and three per cent, and that in the rural counties a decrease of a still smaller amount—about one per cent only. With respect to the causes of mortality, the table shows that, speaking generally, the infectious diseases of children were less prevalent in the recent quinquennium than in the earlier one. There was also a decline in the mortality from syphilis, tuberculosis, and bronchitis. In the aggregate mortality from these diseases there has been a marked reduction during the recent period. Among the causes that contributed to maintain infantile mortality at about its former level were diarrhœal diseases, pneumonia, premature birth, and congenital malformations. The increase of fatality from infantile pneumonia corresponds to an increase in the fatality from that disease at other ages. Taking together the various morbid conditions returned under the head of diarrhœa, the recent five years show a general increase of about 70 per cent; whilst from premature birth and congenital malformations the increase, though numerically smaller, was relatively greater than even that from so-called diarrhœal diseases. In considering the foregoing changes of mortality, the fact must be remembered that the causes of death are now recorded with a much nearer approach to accuracy than

was formerly the case. This would certainly tend to a transfer of deaths from indefinite to definite headings; but the changes of mortality indicated in these comments are so well marked that they probably represent, approximately at any rate, the variations that have actually taken place.

The following table, which relates to one year only, has been prepared to show the incidence of mortality by age and by cause among legitimate and illegitimate infants respectively (*a*) in London, as a typically urban area, and (*b*) in the rural counties of England.

MORTALITY AMONG LEGITIMATE AND ILLEGITIMATE INFANTS, 1902.

Ages at Death.	London.				Rural Counties.			
	Boys.		Girls.		Boys.		Girls.	
	Legitimate.	Illegitimate.	Legitimate.	Illegitimate.	Legitimate.	Illegitimate.	Legitimate.	Illegitimate.
Under 1 week	27·8	41·9	18·8	42·8	29·1	39·6	21·5	31·8
1-2 weeks	7·1	10·9	5·1	12·1	6·4	13·4	4·7	8·4
2-3 ,,	6·8	11·8	5·3	8·6	5·7	9·2	5·2	9·1
3-4 ,,	5·0	11·3	5·0	5·6	4·6	7·4	3·3	4·0
Under 1 month	46·7	75·9	34·2	69·1	45·8	69·6	34·7	53·3
1-2 months	16·0	43·2	12·3	37·1	14·1	25·8	11·4	20·8
2-3 ,,	11·9	36·9	9·6	27·6	10·7	18·7	8·4	14·2
3-4 ,,	11·1	30·6	9·0	19·0	9·4	13·8	6·7	15·0
4-5 ,,	9·4	16·8	7·3	19·4	7·4	11·0	6·0	11·0
5-6 ,,	8·6	18·0	6·4	16·8	6·4	11·7	4·9	8·8
6-7 ,,	8·8	15·5	6·8	16·8	6·1	9·9	5·0	9·8
7-8 ,,	8·4	14·3	6·7	13·4	5·8	8·8	4·6	8·0
8-9 ,,	8·6	11·7	6·8	12·1	5·9	5·3	4·4	6·2
9-10 ,,	7·3	10·5	6·5	10·4	5·4	5·3	4·2	9·1
10-11 ,,	7·5	8·4	6·4	8·2	4·7	5·7	4·5	5·5
11-12 ,,	6·9	7·5	6·7	14·2	3·9	4·6	4·0	4·4
Under 1 year	151	289	119	264	126	190	99	166
Causes of Death.								
Infectious diseases	11·4	9·2	10·5	15·4	8·7	7·9	8·5	8·1
Diarrhœal diseases	20·6	48·6	16·3	47·9	9·0	14·1	6·3	13·9
Syphilis	1·9	19·7	1·1	9·5	·4	3·2	·5	4·0
Rickets	1·0	4·2	·6	1·7	·5	1·4	·5	1·5
Tuberculous diseases	7·9	18·0	6·5	13·8	4·9	6·4	3·3	6·2
Bronchitis	13·5	18·0	10·5	17·3	11·8	15·2	10·5	16·8
Pneumonia	17·1	18·5	13·1	17·7	11·4	13·1	7·8	7·7
Prematurity	23·1	34·4	17·4	33·7	20·3	30·4	15·9	19·7
Atrophy	17·2	50·8	12·8	45·7	20·4	41·7	16·9	36·9

The above table indicates that the waste of life among children born out of wedlock is enormous. This is especially true in London, where they die about twice as fast as do their more fortunate brothers and

sisters. Comparison of the figures for town and country show a great excess in the mortality of illegitimate infants in the town; for whereas in children legitimately born, London mortality exceeds that of the country by about one-fifth part, the illegitimate mortality of London exceeds that of the country by between 50 and 60 per cent. Moreover, there is reason to believe that even this excess understates the truth, for it is known that many pregnant unmarried women whose homes are outside London repair to metropolitan hospitals for confinement, and that the births appear in the London registers. The official records do not show what becomes of either the mothers or their children after discharge from hospital, but most of them probably return to their former places of residence, so that any deaths occurring among these children more than a few weeks after birth are registered outside London. The table further indicates that in both classes of infants the first week after birth is the period of greatest fatality; and also that the mortality in the first month very greatly exceeds that in any subsequent month of the first year of life. The lower part of the table shows that diarrhœal diseases and atrophy cause exceptionally high mortality in the illegitimate; the rate from these affections in London being two and a half times as high in male, and more than three times as high in female illegitimate infants as it is in the offspring of married parents. In the rural counties, too, the mortality from these affections in the illegitimate is about twice as high as that in the legitimate. Syphilis is much the most fatal to the illegitimate, both in town and country; premature birth and congenital defects also cause in them excessive mortality, especially in London. As might have been expected from their surroundings, the offspring of unmarried women fall victims in undue proportion to tuberculous diseases, as well as to respiratory diseases, and to diseases of the nervous system.

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J. T.

ANTHROPOLOGY AND MEDICINE

By John Beddoe, M.D., LL.D., F.R.S.

Our knowledge on this subject is scanty and far from clear; and the little we believed ourselves to possess has been disturbed by recent changes in pathological theory. Divers diseases formerly supposed to be the outcome of constitutional and hereditary proclivity are now believed to be the results of infection; and the remoter causes are apt to be neglected in the consideration of etiology.

That many pathological processes are known to be common to mankind and to other mammalia, or even to animals further removed from us, while others are reasonably suspected to be so, makes it *à priori* improbable that any great differences should subsist in the distribution of diseases among different races of men. On the other hand, though men and women respectively can hardly be said to have any peculiar and exclusive diseases (except in so far as this results from the differences in their sexual organs), yet we see that their respective liability to some at least of these diseases varies. A curious instance of this is afforded by cretinism and goitre: goitre being much more common in women than in men, while cretinism is pretty evenly distributed—if anything there is a preponderance of male cretins.

The most conspicuous difference in the external aspect of men and of races of men is in colour; and here comparative pathology would lead one to look for some corresponding differences in susceptibility to disease, for the experience of horse-breeders and veterinarians is pretty clearly expressed on this point. Thus Youatt says that the dark chestnut, as a rule, yields to no other colour in any quality; but that the light chestnut, which appears to be the analogue of the sanguine-blond man, is spirited, but irritable and delicate in constitution. Black horses, again, number among them some of the very finest of their species; but many of them are heavy and dull in temperament, and there is an idea afloat that they are particularly liable to malignant disease. Here we may be led to think of the choleric and the melancholic temperaments. Among breeds of sheep, the black-faced have the reputation of being hardier than the white-faced. Certain black pigs, according to Darwin, can eat with impunity what would be poisonous to white ones on the same pasture; and like differences are seen in black and white rats. On the whole, the deposition of pigment in the skin and hair of mammals would seem to be the result of processes which connote or accompany health and vigour rather than the opposite.

The statistics of morbidity and mortality, which alone could yield a sound foundation for generalisations on this subject, are unfortunately imperfect, or altogether wanting, in the regions where the material would

be most valuable—those regions, namely, where nations of different colours and constitutions of body live side by side under comparable conditions. In fact, we have hardly any trustworthy statistics, except from the most civilised of the countries, whose populations are compounded from more or less distinct divisions of the human race.

Much information, more or less trustworthy, as to the distribution of disease among different races, may be gleaned from Hirsch, Lombard, Boudin, Oesterlen, Bordier, etc.; but even where the facts can be relied on, they are generally capable of interpretations that make them of little value for our purpose. Thus, when we learn that aneurysm is four times more common in San Francisco among foreigners than among native Americans, we must remember that a far larger proportion of the foreigners are males in the prime of life, and that most of the hard bodily labour is performed by foreigners.

Negroes are said to be exempt, or nearly so, from piles and from varicose veins, and the cause assigned is the greater strength, in them, of the walls of the blood-vessels. Apoplexy, on the other hand (using the word in the ordinary sense), appears to have no racial preferences. Thus, in New Orleans negroes and whites are said to die of apoplexy in the proportions respectively of 103 and 91. In Europe, England, Scotland, Prussia, and Italy yield almost exactly the same figures for death by apoplexy: in all of them these vary between 10 and 11 per 10,000 living; Switzerland and Holland yield 8·5 and 7·9, but Ireland only 5·9. The Irish in America, however, in the year 1900, died from apoplexy and paralysis at the rate of 13·3 per 10,000, a rate higher than that of any other race except the negroes, whose rates for the three age-periods, 15-44, 45-64, and 65 and onwards, compared as follows with those of the Irish and the Germans:—

Negroes	3·2	32·9	127·5
Irish	2·7	30·1	114·0
Germans	2·0	18·8	96·4

Among the Italians at home (*Ann. stat. Ital.* 1898) the average for 10 years was 10·3; in the United States only 2·8, and for the three age-periods, 1·1, 12·4, and 74·4. The Italian immigration into the United States is recent, and has constituted a population extremely prolific and in the prime of life. But the comparison of the Irish and the Germans (strictly speaking, the Irish-mothered and the German-mothered) is a fair one. There must be something far wrong in the mode of life of the Irish-American, as will be seen subsequently. The deaths from brain disease of all kinds, as returned, are singularly few in the insular parts of Scotland and in the Highlands, where the inhabitants are in blood very near akin to the Irish, so that here one might have supposed one had lighted on a real case of hereditary exemption, or at least favourable hereditary constitution; but the fact that Shetland, where the race is Norse, returns fewer deaths from brain disease than even the Highlands and the other islands, is sufficient to negative the idea that the Gaelic

race has any such special immunity. The rate of mortality from this class of diseases is certainly lower in quiet rural districts than amid the hurry and worry or excesses of towns, and this may account for some degree of the apparent immunity; the remainder must be attributed to the tendency to set down all cases of death in advanced life to simple "old age." In Shetland and the Hebrides about 25 per cent of the deaths are thus certified.

In cancer, again, the enormous differences in mortality reports are doubtless largely due to the non-recognition of internal growths. But the differences reported to exist in divers registration districts in England seem too great to be wholly due to this cause, and the extreme variations in both directions are by no means such as would have been expected on such a hypothesis. For example, rural districts in general seem to suffer quite as much as cities, and ancient cities more than great centres of industry, even allowing for the difference of constitution of the population in respect of age. [Haviland.]

There is some little ground for considering cancer to be a disease of civilisation, or of civilised communities and races, though here of course the question of failure in diagnosis comes in with double force. The most formidable death-rates that we have, such as 990 per million living in Drontheim, 930 in Lombardy, and 928 in the French-mothered people of the United States, come from highly civilised communities. In Switzerland indeed, a country which yields to no other in true civilisation and the well-being of its population, the numbers have in recent years been still more alarming. Cancer is said to be rife in China, but rare in Egypt, the scene of a yet older civilisation. In the United States, however, the death-rate of Chinamen by "cancer and tumour" is put at 494 in the million, that of whites being 667, of negroes 480, of Amerindians 286, of Japanese 240. I have no information as to the ages of the Chinese and Japanese, but I apprehend that they are all or nearly all in the prime of life, while the whites, negroes, and Amerindians are of all ages. Now the average mortality of whites from 15 to 44 years is put at 238, which makes the Chinese rate appear very high, and the Japanese one doubtful. It is thought to be uncommon in the negro race generally, whereas we have seen that it is prevalent in Norway, among one of the blondest populations in the world. The asserted rarity in Iceland may perhaps be remanded for further evidence; could it be proved, it would be of great importance, the Norwegians and Icelanders being of the same race. That the disease is strongly hereditary scarcely any one doubts[1]; and I shall presently submit some evidence to show that in Britain it is especially common among people of dark complexion.

Gout is another strongly hereditary disease, common in certain races and communities, but very rare, perhaps non-existent, in others. Roughly speaking, it is a disease of the ruling races and the higher

[1] This statement may be thought too strong at the present time; but those who deny "heredity" cannot deny "hereditary proclivity"; it is little more than a question of words.

classes; of the civilised man, not of the savage; of the white man, not of the negro; of cold and temperate rather than of hot climates. Probably there exist large communities of men among whom it never occurs; but, given some of the requisite exciting causes, habitual but not extreme excess in eating and drinking, disproportionate use of the brain as compared with the muscles, consumption of certain kinds of drinking-water, etc., it could doubtless be produced in any race and in almost any climate. Negroes, as I have said, are generally free; but Lobengula, the famous king of the Matabele, drank much beer, and suffered severely. The reported distribution of the disease is very instructive. Thus, in India, it is said, the Hindus scarcely ever suffer; the Mussulmans, freer in diet, sometimes. Gout occurs in China, where the mandarin class unite most of the requisite factors. In Madagascar, the comparatively clever and light-complexioned ruling race, the Hovas, suffer from it; the subject negroes are not known to be attacked. In the United States of America it occurs in the cities, but is little known elsewhere; the American farmer is active and temperate.

The registered death-rate from gout in England is about 18 per million living, in Scotland it is 4·3 per million, in Queensland, where much more fresh meat is eaten than in England, about 5. The chief missing factor is probably beer; but at least we are justified in saying that in these cases differences of regimen and climate reduce the mortality in the same race to less than one-third.

Still, it must be acknowledged that the distribution of gout has a racial aspect. In France, according to Hirsch, Lorraine, Normandy, and Lyons are said to be its chief pasture-grounds; others add Burgundy and blame the wine. The natives of all these districts have more or less of the Germanic element in them. In Spain, the least Iberian of Spaniards, the Asturians, are the most gouty. The Belgians, the Dutch, the Danes, the Northern Germans, the Upper Austrians, and, in Russia, the upper classes of St. Petersburg and the Baltic provinces (Germans again) are all said to suffer from it. If there be one thing which all these people have in common, it is that fondness for heavy feeding which has been a characteristic of our own most gouty nation from time immemorial, and belongs particularly to the true Saxon-English type.

Pulmonary Tuberculosis has always been a sort of battle-ground for the believers in infection, and the believers in hereditary transmission and the susceptibility of particular types. Until quite recently, though the former opinion ruled in Southern Europe, the latter was almost universally held in England. But though even now clinical and practical experience point in the same direction as formerly, the general and geographical history of the disease seem to support the now prevailing infective theory. The effects of local conditions of soil and climate, though undoubtedly very powerful, are not always distinct, and may be used in support of either view.

The local statistics of pulmonary tuberculosis are of very great interest, and could not, of course, be dealt with satisfactorily within the compass

of this article. Some of them seem to point to the applicability to pulmonary tuberculosis of the "virgin soil" doctrine, which at first sight seems incompatible with that of the importance of heredity.

Among the more important points which may be taken as established are—

1. The extreme rarity of pulmonary tuberculosis at very high elevations.

2. Its rarity in high latitudes: for example, in Iceland.

3. That some of Haviland's conclusions as to local mortality are correct—for example, that damp clayey soil coincides with a high phthisical death-rate [Bowditch, Buchanan], and that the warm, fertile, ferruginous red-sandstone tracts of country are most remarkable for low death-rates; a "sheltered position and a warm, fertile soil, well drained, being coincident, as a rule, throughout England and Wales, with a low mortality from phthisis."

The following opinions may be put forward more doubtfully:—

1. That among bodily characters, tall stature is the most distinctly unfavourable. Dr. Shrubsall, in his extremely valuable paper on "Physical Characters and Morbid Proclivities," contests this point, the principal evidence for which is contained in the statistics of Dr. Boyd, and those of the American Civil War. Dr. Shrubsall's own observations, extending to 1000 individuals in Brompton Consumption Hospital, are sufficient to render the matter doubtful, but not, I think, to do more; for it may be questioned whether the mean stature he found (about 5·59 feet = 1674 cm.) is not quite up to the standard of the somewhat degenerate population of Londoners from which his material was largely drawn. They would suit, I think, the hypothesis of two or more types, one the tall young man who has "overgrown his strength," another the stunted degenerate who succumbs to the disease later in life.

2. That though local situation, varieties of social habit, occupation, and the like, overbear and obscure in Britain anything like racial tendency, it would appear that the Gaelic and Kymric or Ibero-Keltic stocks are, *cæteris paribus*, rather more subject to pulmonary tuberculosis than the Saxon and Scandinavian. (The principal objection to this statement is furnished by the very unfavourable position of Suffolk, one of the most purely Anglian counties.) Dr. Shrubsall thinks that "this position could be placed more strongly"; and he adduces a large number of observations of his own, from several districts or localities, which strikingly corroborate my own. So do the results of the American census of the year 1900. Thus:—

[Table

REGISTRATION AREA OF UNITED STATES, 1900.

DEATH-RATES BY AGE, COLOUR, AND BIRTHPLACE OF MOTHERS, IN 100,000 LIVING, OF PULMONARY TUBERCULOSIS.

	Ages.			
	0-15.	15-45.	45-64.	65+.
Ireland	42	428	341	325
Scotland	33	201	202	238
England and Wales	27	151	173	234
Scandinavia	32	234	267	236
Germany	26	206	207	235
United States	27	162	132	176
Italy	51	150	157	145
Coloured	246	587	518	549

Here the deaths of the Irish from pulmonary tuberculosis are enormously in excess of those of the Germanic and other white races. It must be considered that (i.) they cling to the cities and city life; (ii.) they are the most addicted to alcohol of the races concerned; (iii.) they are found most numerously in unhealthy occupations, as publicans, clerks, general labourers, printers, masons. Still there would seem to be something more, something in the constitution of the race. In Queensland, too, they suffer more than other whites.

3. That the tropical negro is particularly subject to pulmonary tuberculosis, at least when removed from his own country. The Melanesians, or Oriental or Pacific negroes, may be here included; these are the people, incorrectly called Polynesians, who work in the Australian sugar-fields, and though well fed and fairly lodged, die of consumption in very large proportions—

DEATH-RATE FROM PULMONARY TUBERCULOSIS IN QUEENSLAND, 1890 and 1891 [BLAKENEY].

"Polynesians" per 1000 living	16·76
Chinese	1·17
Europeans and Colonials	·98

It is needless to cite statistics of the decimation of the true African negro in other climates than his own. In some cases the figures are even more appalling than those I have quoted from Queensland; and in some of the countries into which negroes have been introduced they seem to melt away chiefly from this cause. The most remarkable exception to the rule is that furnished by the southern portion of the

United States of America. Here, though within the temperate zone, a negro peasantry has been firmly established, thrives and multiplies. It is even said that the death-rate from pulmonary tuberculosis in the Southern States generally is lower among the blacks than the whites.[1] If it be so, it is because the former are the peasantry, and a fairly well fed and lodged peasantry, with a wholesome amount of bodily labour; whereas the whites are generally inhabitants of towns and villages, with inferior conditions of life, *quoad* liability to pulmonary tuberculosis.

The mortality from this disease waxes and wanes in different countries in a manner that invites speculation on the causes of change. England and Holland used to be thought its special seats. But now for a considerable time pulmonary tuberculosis has been on the wane in England,[2] and the death-roll therefrom in the cities of France and Germany and Northern Italy has been growing or becoming more visibly formidable. It has also grown in Scotland coincidently with the growth of urban population, and with what has been regarded as improvement in the dwellings of the rural population. In North Germany the western provinces yield heavier rates than the eastern; and here too, though some might rely upon the racial difference between the true German and the Slav, I believe the real difference to consist in a rather more elaborate civilisation, which brings with it air-tight houses and other fair-seeming but really evil conditions.

Yellow fever is one of the most selective and fastidious of diseases; almost as much so as the sweating sickness of the Middle Ages, which on its first appearance is said to have sought out the well-to-do and lusty Englishman, abroad as well as at home, and let the starveling and the foreigner go scatheless. In New Orleans, for example, there is said to be a regular scale of exemption, complete in the case of the full-blooded negro, less in the mulatto or other man of colour, less still in the dark-complexioned creole of Spanish or French descent; while even the Southern European suffers less than the Englishman, and the Scandinavian fares worst of all. This sounds a little too artificial; but all agree that the dark skin connotes a kind of acclimatisation to the scourge similar to that which long residence confers. We have here, perhaps, the most conspicuous instance of race peculiarity in disease, the hereditary anomalies of pigmentation in the negro being clearly connected with his exemption from a disease in which that function is much implicated. The yellow colour of the fat in the negro, and the comparative whiteness of the stools, should be remembered in this connexion.

Now that we know so much more about the genesis of "malarial fever" than we used to do, it is not so surprising to learn that in America, in the United States in the year 1900, the death-rate from this cause was nearly ten times as great in the coloured population as among the whites.

[1] In the Northern States (the "registration area") it is very different, as has just been shown.

[2] Partly, no doubt, from a change of name, but not mainly so. The great increase of deaths registered under bronchitis and pneumonia has been at other ages than those at which pulmonary tuberculosis has decreased.

Scarlatina is much milder and less formidable in Southern than in Northern Europe. More than one reason suggests itself for this; but the greater frequency of enlarged tonsils in the lymphatic temperament, which is so common in North-Western Europe, supplies one of these. In America the negroes suffer less from scarlatina than the whites; and the Italians have no immunity.

Small-pox is exceedingly fatal to peoples among whom it is introduced for the first time. No doubt this is partly owing to terror at the appearance of a new and dreadful enemy, and to ignorance of proper methods of treatment, etc.; but we can hardly doubt that it is also connected with the fact that any such organism flourishes best in a virgin soil. The frightful amount of destruction of life by small-pox among the North American Indians, especially on its first introduction, can hardly be accounted for in any other way. Thus the Mandan nation was almost destroyed; it has even been stated that in their principal village only forty out of 2000 survived the invasion; but it has never been asserted, so far as I am aware, that with vaccination and proper care the Indians suffer more from small-pox than other races. To show that other races suffer almost equally under similar conditions, we may quote the earliest epidemic of small-pox in Iceland, when 18,000 out of 52,000 were said to have perished. Some facts of this sort might lead one to suspect that past diseases may exercise some kind of protective power against others, even when their relation is much more distant than that of vaccinia to variola. Thus we hear of the discovery of a village church in Tellemarken (Norway), whose very existence had been forgotten, the entire population of its remote parish having, there is reason to believe, been swept off by the black death. In this case, probably, the soil was virgin to many other diseases besides this particular pest: or is it that a population which has not been sifted through the meshes of other zymotics is more vulnerable than another, though apparently more healthy?

Whether the virgin-soil hypothesis be necessary to explain the occasional destructiveness of measles, may be doubted. Though on its introduction to Fiji it killed about a fourth of the population, it is said not to have been extraordinarily severe among those Fijians who were carefully nursed in European fashion, and protected from their own folly; the mortality has been quite as great in France under bad sanitary conditions. There is no sufficient reason to think that any one race is more liable to be severely handled by measles than another, under equal conditions. Negroes suffer much more than whites, it is said, in the United States, but in 1900 the Italian children died in much greater proportion, and the Scandinavian and Jewish ones in almost as great a proportion, as the coloured; the difference is only what we find in this country between the upper and the lower classes. Tetanus and trismus neonatorum are supposed to be particularly fatal among negroes; but here again it is probably the habits of the race that are in fault, rather than anything in its physical constitution. One can hardly imagine any

resemblance in the latter respect between negroes and Icelanders; yet the inhabitants of the Westmann Islands, off the coast of Iceland, used to lose the greater part of their infants from trismus, until they were taught by Schleisner to reform their manner of treating them during the first few days of life. Hirsch assigns as a probable cause a peculiar sensitiveness of the negro skin; but the suggestion appears to me unwarranted and gratuitous.

Chorea is said to be unknown in China, and we may probably assume with safety that it is rare. Whatever its relations with rheumatism, it is certainly a disease of the nervous temperament especially. For its physical type see further on. There are several more or less obscure diseases to which negroes seem to be exclusively or particularly liable. Of these is the sleeping sickness, from which, however, we now know that whites are not really exempt. The mysterious ainhum, which resembles a limited leprosy, is not known to attack other races; but yaws certainly does.

Of all white races, the Jews are the most likely to reward a careful study of special morbid tendencies; but I am not aware that this has ever been thoroughly carried out. It is unfortunate that the American Government does not distinguish between the Jews and other natives of Russia and Poland; but in these mixed categories the death-rate from consumption, strange to say, is low, and that from cancer uncertain. Can it be possible that the Jews are getting rid of consumption by a process of natural selection? They are known to have a lower death-rate, wherever it has been tested, than the Christian populations among whom they live; but this may be due simply to their sober habits and carefulness in diet, their avoidance of violent labour, and their great care of their children. They are believed to suffer much from diabetes, from nervous diseases, and from psoriasis.

If we now regard the subject from a geographical point of view, we shall be able to make use of the gigantic series of anthropologico-medical statistics which we owe to Dr. Baxter and to the American Civil War. Perhaps the clearest and most important fact that comes out of them is the inferiority of the blond-complexioned man for recruiting purposes. Out of twenty-two principal classes of physical defects, twenty of which imply disease of some kind, in only one, chronic rheumatism, did the dark-complexioned recruits yield the larger percentage of rejections. As De Candolle says, the very uniformity of the thing is somewhat suspicious. He suggests that it may be largely if not wholly due to the inclusion of great numbers of Germans, the German emigrants being often of inferior physical type. Other possible sources of fallacy suggest themselves to me; for example, it is conceivable that the blond element, more courageous and adventurous as a rule than the brown, may have been more disregardful of its physical drawbacks in volunteering; but it must be allowed that a *primâ facie* case was made out against the blonds. The excess of blonds was most marked in the rejections for pulmonary tuberculosis, and for diseases of the urinary and circulatory systems. Dr. Baxter says there was an excess of dark men

among the few rejections which took place on account of certain acute diseases, of cancer and of chronic rheumatism. To this point we will return presently.

I have made out a list from Dr. Baxter's data, showing in relative order what appeared to be the weakest points in recruits of several nationalities and races :—

1. White men born in the United States were frequently rejected for diseases of the digestive and urinary systems, for bad teeth, and for pulmonary tuberculosis.
2. American Indians for *nothing* ; they were the soundest of all the nationalities, as well as the tallest and largest in girth.
3. Negroes—For urinary diseases. Also very healthy ; but were probably picked men.
4. British Americans—For nothing specially ; generally very healthy.
5. Mexicans—Diseases of the nervous and cutaneous systems, syphilis, diseases of the locomotive and generative systems, and local injuries.
6. South Americans—Syphilis and respiratory disease.
7. West Indians—Urinary disease.
8. Englishmen—For bad teeth, and for affections of the digestive organs.
9. Scotland—Diseases of the circulatory, urinary, and digestive systems.
10. Ireland—Diseases of the circulatory system, of the skin, and of the digestive system ; syphilis.
11. Wales—Pulmonary tuberculosis, and diseases of the urinary and locomotive systems.
12. France—Diseases of the skin and the nervous system ; bad teeth.
13. Holland—Pulmonary tuberculosis ; diseases of the skin, eye, and ear, and of the respiratory and locomotive systems ; and local injuries.
14. Germany—Pulmonary tuberculosis ; diseases of the circulatory and locomotive systems, of the ear, and of the digestive system.
15. Sweden—No morbid peculiarity ; very healthy.
16. Norway—Diseases of the ear and of the locomotive system.
17. Denmark—Diseases of the eye.
18. Switzerland—Diseases of the urinary system ; defects of the teeth, of the ear, and of the digestive system.
19. Portugal—Hernia ; diseases of the digestive and generative systems.
20. Italy—Diseases of the skin and of the generative system ; syphilis.
21. Russia—Diseases of the eye, of the nervous, circulatory, and generative systems.
22. Hungary—Diseases of the digestive and nervous systems, of the ear, of the generative and respiratory systems ; hernia, and pulmonary tuberculosis.
23. Poland—Diseases of the eye, and of the circulatory and respiratory systems ; pulmonary tuberculosis, and local injuries.
24. Spain—Diseases of the respiratory organs ; syphilis, hernia ; diseases of the generative and digestive systems, and of the eye.[1]

This list, like the results of most voluminous collections of statistics, is after all a little disappointing. It is not easy to draw any important

[1] The numbers examined were small in the cases of the Indians, Mexicans, South Americans, Spaniards, Portuguese, Russians, Hungarians, and Poles.

general conclusions from it except perhaps this, that the native and naturalised races of North America stand better than the recently imported. Thus the red-skins, the aborigines, stand best; and nearly as well stand the West Indians, the coloured men of the States, and the British Americans—mostly, I suppose, French Canadians,—a hardy, unsophisticated peasantry, largely crossed with Indian blood.

Respiratory disease is found rife among Spaniards and South Americans, but not, as might have been expected, among Mexicans, West Indians, or Portuguese. The numbers were perhaps insufficient, except in the case of the West Indians. The correspondence between this list and the death-roll of the United States thirty years later is by no means striking. Thus neither Italians nor Irishmen appear to have been numerously rejected on account of diseases of the respiratory system: yet both are distinctly more subject to death by them than any other race except the negroes.

Dr. Baxter makes a remark on a certain relation, signs of which appear in some of his tables, though not in my abstract of them. It is a sort of general resemblance in the nosology of the British races, among whom, I think, he means to include the American whites, as compared with the other races observed. He found the proportion of rejections to increase with age and with height. To some small extent the latter fact was due to the former one, but the increase of pulmonary tuberculosis with a stature beyond 65 inches was far too great to be accounted for in that way. The same may be affirmed of cardiac disease and varix, both of which appear to increase rapidly with increase of stature.[1] Hernia, however, contrary to the opinion of Boudin, does so very little, or not at all. General debility, as a cause of exemption from service, decidedly lessens with increase of stature.

In all these there is a distinct, though not very great excess of men of light complexion. There are, however, a number of morbid conditions entailing rejections, the majority of the sufferers wherefrom are set down as dark, though none of these are of great importance numerically. Most notable are dropsy, cancerous and other tumours, cataract, certain defects or affections of the nervous system—as imbecility, neuralgia, chorea—chronic alcoholism, chronic pleurisy, and certain affections of the portal system, as liver disease, hæmorrhoids, and prolapsus. It may be noted that most of these are precisely the vices of the "melancholic temperament."

Next in value, for our purposes, to the great American statistics are those of the French recruiting service; not so much for their intrinsic importance as for the light thrown upon them by Boudin and Broca, and by the investigations of Topinard into the distribution of complexions, and by those of Collignon into that of head-form in that country. Moreover, great as is the assimilative power of the French nation, its principal anthropological types—the Kymric, the Keltic, the Mediterranean, the Norman, etc.—still remain tolerably distinct.

[1] Dr. Shrubsall found a stature of 66·94 inches (1700 mm.) in 50 patients with heart disease, that of as many cancerous persons being only 64·8 (1646 mm.).

French anthropologists generally take the view that the Norman and the Kymric types are but varieties of one—the tall, blond, long-headed North European type; and that this, so far at least as it appears in France, is characterised not only by these three qualities, but also by tendency to chest disease, to dental caries, to varices, and to some other affections, from all of which the short, thick-set, dark, broad-headed Kelt of the central provinces is comparatively free. The southern and south-western portions of the country are occupied partly by the last-mentioned race, but partly by short, dark, long-headed people, often classed together for convenience as the Mediterranean or Iberian race, but probably capable of analysis into more than one type or stock, not to speak of various admixtures added during the historic period [Collignon]. We should therefore have in the French recruiting statistics an opportunity almost unequalled of testing the comparative morbidity of different types of man, and the nature of hereditary morbid tendencies, could we rely on the carefulness of the medical examination of recruits. Unfortunately, however, there is intrinsic evidence that, during the period for which statistics are published, this used to be by no means sufficiently careful and systematic. For example, it was the practice usually to measure the conscripts, and reject those under size, before investigating the other possible disqualifications. Of course this plan, otherwise unobjectionable, had, from the medico-statistical point of view, the disadvantage that the infirmities of the under-sized men were not disclosed or tabulated, and that those departments which yielded a large proportion of small men did not exhibit in the reports their actual proportion of myopia, chest disease, and so forth, but only the proportions occurring in the taller men. But sometimes this order seems to have been reversed, with the effect of assigning to the department or commune under examination too high a stature, but its full proportion of infirmities. These things must be borne in mind in the examination of the table which I have constructed in order to exhibit the relative morbidities of several groups of departments, selected on anthropological grounds. The column headed "Do. probable, corrected," is the result of an attempt to neutralise the errors resulting from these defects of method. Though conjectural, I have no doubt it comes much nearer to the truth than the official statement. Boudin's book was published when France had eighty-six departments; she subsequently gained three, and then again lost other three, so that the number is once more eighty-six. In forming my table I have always taken the several departments in what may be called the order of excellence; thus, under the column of "Dolichokephaly" No. 1 would be the department with *most* long-headed men; under that of "Mortality" No. 1 would be the department with the *lowest* death-rate, No. 86 that with the highest; under that of "Myopia" No. 1 would be the department with the *fewest* short-sighted youths, and so forth. In making my groups I have thrown together the ordinal figures belonging to several departments, and set down the average in the table. Thus, in the case of the ten departments yielding the tallest men (or rather the fewest

under-sized men), I set down 5. But the order in which they produce tall men is slightly different from that in which they are free from dwarfs, so that the average position of these same ten, in that column, comes out as low as 12.

Bertillon's order of mortality also requires explanation. Instead of assessing the mortality simply on the aggregate population of all ages, Bertillon calculated the death-rate for each of twelve age-periods on the population living at such ages respectively, and averaged the several orders thus obtained in order to get the proper rank of the department. The result is sometimes a startling change in its position. Thus the Seine-et-Marne stands fifty-fifth on the ordinary plan, with a death-rate of 23·5. This low position is really owing to the great number of children sent out from Paris to be nursed in this neighbouring department, who sustain a frightful mortality. The ultimate rank of the Seine-et-Marne, on Bertillon's plan, would be the twenty-third; the average of its several ranks, which I have chosen for use in my table, being 29. The Seine-et-Oise similarly leaps from the sixty-fifth to the fortieth place, with an average rank of 41. Indre, where the infant mortality is low, falls from tenth to fiftieth, with average 49, and Creuse from sixth to fifty-first, with 50.

The table (p. 94) is full of instruction, and yields, on examination, some valuable and unexpected results, of a nature not directly germane to our inquiries. Thus, the very pregnant fact comes out that high mortality and military inefficiency—or unsound health from the recruiting-officer's point of view—stand in no direct relation to each other: in truth the relation is very frequently inverse. Thus, of all my fifteen categories the Breton departments stand worst in regard to mortality, but best by far in point of soundness; while the ten thinly-peopled low-country departments have the worst rate of exemption for unsoundness, but, with one exception, the lowest rate of mortality.

The most promising lines of investigation for us, however, are those afforded by pulmonary disease (including especially tuberculosis), by mental derangement, by myopia, and by defects of the teeth.

Of these the first, as we have learned already, has some relation to tall stature, and this law is borne out by our table, wherein the departments of highest stature take the forty-eighth rank, but those of lowest stature the thirty-fourth. There appears no evidence that blond coloration, *per se*, has any unfavourable influence; the comparatively blond Lorrainers, for example, standing very well in this as in most other respects, and the dark Provençals very badly. The great towns stand ill, of course; but when we find that the ten departments where the northern dolichokephalic race is most in evidence, and the five of Normandy, and the five which I have selected as best exhibiting the combination of tall stature, long head, and blond complexion,[1] agree in yielding a high average of phthisical recruits, little doubt remains in my

[1] Viz. Pas de Calais, Somme, Aisne, Oise, and Calvados, the last only a Norman department. I excluded Nord and Seine Inférieure as having a strongly urban character.

TABLE ILLUSTRATIVE OF THE DISTRIBUTION OF DISEASE IN FRANCE, CHIEFLY FROM RECRUITING STATISTICS.

									Exemptions for						Exemptions for				
Number.		Order for high Statures.	Do. low, do. exemptions.	Dolichokephaly.	Blondness.	Mortality.	Do. (Bertillon).	Do. 0 to 5 years.	Infirmities.	Do. probable, corrected.	Phthisis and Respiratory Diseases.	Weak Constitution.	Scrofula.	Mental Alienation.	Hernia.	Myopia.	Epilepsy.	Mutism.	Defective Teeth.
1	10 Departments of highest stature	12	5	49	22	33	32	40	49	41	48	44	29	0	36	38	35	41	57
2	10 Lowest stature .	76	81	35	60	49	57	38	42	52	34	59	40	–	40	27	32	50	31
3	10 Most blond .	23	23	28	5	51	42·5	38	40	37	46	42	40	+	33	34	43	50	53
4	10 Darkest . .	56	46	33	81	50	45	51	35	35	49	35	31	– –	42	50	62	55	45
5	10 Dolicho northern	18	19	12·6	17	57	42	54	57	51	54	47	42	0	49	48	48	42	71
6	10 Do. southern or western . .	64	60	9	62	48	53	49	42	46	43	51	22	–	60	54	43	45	42
7	10 Brachykephaly .	38	35	81	52	40	43	38	41	40	33	47	56	0	41	45	43	59	32
8	9 Auvergnat race .	60	71	72	63	60	55	52	30	39	27	43	66	–	20	32	44	58	15
9	5 Normans . .	28	26	20	6	43	35	35	62	59	54	55	40	+	45	50	32	43	73
10	4 Bretons . .	74	71	41	28	69	65	41	6	21	22	17	27	–	3	6	41	41	9
11	5 Remo - Lothrin - gians . .	22	14	61	16	26	25	35	39	30	24	41	46	+	43	46	43	48	48
12	6 Urban . .	34	28	25	42	61	59	55 +	49	45	62	45	49	+ +	51	62	46	29	54
13	5 Tall, dolicho-blond combined	12	13	15	15	45	33	54 –	55	47	55	50	40	+	37	36	46	39	73
14	10 Mountaineers .	51	48	58	56	53	50	47	42	43	41	32	48	– –	38	49	41	50	36
15	10 Thinly - peopled low-country .	45	46	34	44	29	35	44	62	60	51	54	48	–	52	43	38	37	50

The materials for this table are derived from Boudin (*Géographie médicale*, 1857), from Broca, from Topinard (*Anthropologie générale*, 1885, and *Revue d'Anthropologie*, 1889), and Collignon (*L'Anthropologie*, 1890); and from Bertillon père's *Démographie de la France*, 1875.

The number of departments being eighty-six, the normal or mean position is 43·5.

The urban mortality, especially that from 0 to 5 years, is understated, and that of No. 13 perhaps slightly overstated, by reason of the number of town-born and especially Paris-born infants who die in the country.

In the column "Mental Alienation," 0 represents about the average of France, + an excess, + + a large excess, – a deficiency, – – a large deficiency of insane persons, as compared with the average. Bordier, quoting Chervier, gives a list of departments in which mental alienation is common, and in which no Norman, and no strongly urban district appears.

mind that we have to do with an affair of race or heredity. This is in some degree confirmed by the Belgian statistics, which exhibit the Flemings and Brabançons as yielding more tall recruits and more cases of pulmonary tuberculosis than the Walloons [Vanderkindere, Houzé]. Here, as in other parts of our subject, cause and effect are almost inextricably confounded; and, in order to understand the problems, the local history and conditions must be studied. Thus in France—

Of 10 brachykephalic departments, only 1 has more than the average density of population.			
Of 10 Northern dolichokephalic departments,	10 have more.		
Of 5 Norman	,,	5	,,
Of 4 Breton	,,	4	,,
Of 10 Most blond	,,	9	,,
Of 10 Darkest	,,	3	,,
Of 10 Southern dolichokephalic	,,	2	,,

We in England, with our almost unchequered experience of higher death-rates from pulmonary tuberculosis in cities than in rural districts, would be inclined to say at once, "Here, in the greater density of population, is the one and sufficient reason for the greater amount of pulmonary tuberculosis in recruits from Flanders and Picardy and Normandy!" This would be too hasty a conclusion. In France, as my table shows, the hard-wrought, ill-fed peasantry of the plains suffer much from tuberculosis. The peasantry of Limburg, the most Germanic province in Belgium, and perhaps the most rural except Luxemburg, stand about the worst in this respect. On the other hand Bretagne, the part of France least affected by pulmonary tuberculosis, has, as we have seen, a dense population, though no *very* large town.

The fact is, the tall, long-headed blond population is where it is by reason of its physical and moral qualities, its striving, ambitious, masterful character, which enabled it to occupy the best and most fertile parts of France, leaving the hills and heaths to the dark, short-headed Kelts.

Mental alienation has not the same distribution as phthisis and pulmonary disease, which seem to affect the dark southern or Mediterranean race as much as the fair northern one, sparing only the sturdy, dark, broad-headed people of the centre, and the anomalous Bretons. The number of the insane seems to be large throughout the blond area,[1] where it is probably a race-character; and also, of course, in the districts of the great cities. We should not forget, of course, to allow for the influence of alcoholism, which is much greater in the north of France than is generally supposed, and has been increasing.

It has been affirmed that myopia is structurally connected with dolichokephaly, the deep orbit and the long-axed eyeball going naturally with the long head. A certain amount of evidence has been adduced in

[1] I draw this inference from Boudin's figures, vol. ii. pp. 235-37; but they are perhaps hardly sufficiently detailed, though very striking.

support of this idea; and the tall blond race has been saddled, in the minds of some anthropologists, with yet another hereditary defect. The evidence of my table is not conclusive either for or against this view, but it certainly does something to render it unlikely. Of the five departments selected as representative of the type, one only, the Aisne, had an excess of myopes; and of the ten most blond departments only two, viz., Eure and Seine Inférieure, both very urban. In fact, myopia distinctly belongs to the dark-eyed inhabitants of the south of France, and to those of the cities, with the strange exceptions of Lyons and the urban district of the Nord: Brachykephals have their full share of it.[1]

The subject of defective teeth would, of course, furnish material for a goodly volume. So far as my materials testify, good teeth in France go with short average stature, dark complexions, and, less distinctly, with broad heads. Bad teeth concur with tall stature, and almost as clearly with long heads and blond complexion. Or, to put it in another way, teeth are good in the mountains as a rule, bad in the plains, and especially bad, as Boudin himself remarked, around the mouths of all the great rivers. They are good among the Auvergnats (or central Kelts), and especially so among the Bretons; also in the Catalans of Rousillon, etc.; bad among the northern blond long-heads (including the Normans), and among the Gascons; moderately good among the Ligurians. In all these cases the boundaries are pretty clearly drawn, so as almost irresistibly to suggest that either the hereditary constitution of the several races or kindred, or something in the local (may I say tribal) habits and customs must have to do with the phenomena. For example, the Loire Inférieure was formerly politically a part of Bretagne, but its people were not Bretons in blood and customs. Accordingly the Bretons have a very high mortality and very good teeth; the Nantese, or Lower Loire folk, have a low mortality and very bad teeth. On the other hand, the neighbouring department of Mayenne was not Breton politically, but its people are said to resemble the Bretons in character. Accordingly they have a rather high mortality and excellent teeth!

This connexion between good teeth and a high death-rate is strange, but unquestionable. Of the ten departments which furnish the fewest exemptions for defective teeth, every one has an excessive mortality, and in most cases, and on the average a very excessive one. They are all in two classes, viz. 1. Auvergne and Lyonnais; 2. Bretagne with Mayenne. If we seek for dietetic causes of caries, we shall find that the great wine-producing districts, Gironde, Dordogne, Marne, Côte d'Or, as well as the cider-drinking Normandy, are among the worst on the list. But, after all, there is plenty of sour wine in Auvergne and of cider in Bretagne.

On the whole, then, I am disposed to subscribe to the belief of the

[1] At Cambridge, the kephalic index of 200 myopes averaged 78·77, the whole series of men observed giving 78·96, a difference not beyond the limits of probable error (Beddoe, *Sur l'histoire de l'Index Céphalique*, dealing with Dr. Venn's data).

French anthropologists, that we have here another example of a hereditary and constitutional defect. But it is one which cannot be dated back indefinitely; it must have been developed on French soil. Even now the Scandinavians, the purer-blooded cousins of the northern French, are generally "euodont"; and it is certain that when the Saxons invaded England, and the Franks and Normans Gaul, they were still so. If Harold of Denmark, the conqueror of the Cotentin, had not been a singular exception, he would hardly have been nicknamed Blue-tooth.

In the British Isles we have no such groundwork of statistics to work upon as those on which I have been building from America and France, and I have little more than personal observation whereto to trust. This, however, is sufficient to enable me to assert that pulmonary tuberculosis is not here, as some have supposed, especially prevalent among blonds.[1] The proportions of the several colours of hair and eyes in the sufferers are not very different from those which obtain in the general population. If anything, there is even an excess of black and very dark hair. Some statistics given me by Dr. Edward Liddon of Taunton, from the Brompton Consumption Hospital, are confirmatory of my own, and Dr. Shrubsall's more extensive and numerous data point in the same direction. I *think*, however (on this point statistics are unavailable), that hereditary phthisis in the upper ranks often presents itself in a frail blond type with very light hair; and I am sure that a fine transparent skin is a sign of vulnerability. In fact, the typical victim of pulmonary tuberculosis is, in my opinion, a tall person with blue eyes, a transparent complexion, and dark hair. Such persons are also more liable to hæmorrhages; it would seem that in them other structures partake of the delicate organisation of the skin.

I have already said, *apropos* of the supposed absence of chorea from the Chinese, that, whatever its connexion with rheumatism, it is a disease specially belonging to the nervous temperament. Fatal and severe cases almost always present the signs of that temperament. There is usually something remarkable about the development of pigment; the hair is often coal-black, but sometimes extremely light, flaxen, or pale red. Epileptics, cataleptics, ecstatics, thought-readers, clairvoyants, are very frequently of one or other of these strongly contrasted colour-types. Dr. Shrubsall finds a high index of pigmentation for both eyes and hair in epileptics. Mania seems to occur rather more often in the xanthous type, with chestnut, red, or fair hair; but with regard to melancholia the observation of the ancients was undoubtedly correct; it belongs especially to the type which they called melancholic. whose outward signs are tall stature, olive complexion, and straight dark hair.

It has been asserted that some races of men, dwelling beyond the domain of statistics, enjoy an absolute immunity from cancer. From what we now know as to the wide extra-human diffusion of malignant disease, this is extremely improbable. More than one hypothesis has been

[1] See analysis of upwards of 1000 cases in *Races of Britain*, pp. 222, 223.

advanced as to the physical constitution which furnishes the best seed-bed for cancer. For example, it has been said to be very common in persons with orange-hazel eyes, or with eyes in which the colour is much mixed or broken, in which the general effect on a distant view is green. My own observations have not confirmed this notion. Cancer, in my opinion, is most common in people who have a fairly healthy constitution in other respects. The prevailing complexion, among the subjects of cancer in this country, is dark. Out of sixty-seven such, English and Scotch, I found eight with black or brown-black hair, and thirty-two with dark brown; thirty-four had light, ten neutral, and twenty-three dark eyes. These figures vary from those of the surrounding non-cancerous population very decidedly in the direction of darkness. Mr. Roger Williams, who has also investigated this subject, and on a somewhat larger scale, has kindly shown me the figures, which bear out my own conclusion. It will be remembered that Dr. Baxter's American statistics also agree with our own on this point. Dr. Shrubsall, after examining and quoting the statistics collected by Wolff and Kruse and others, concludes that the cancer mortality increases in Germany from north-east to south-west, and in Italy from south to north, the intervening Switzerland exhibiting the maximum; and he is disposed to think the Alpine race more liable than the Teutonic. As to complexion, Dr. Shrubsall agrees with the rest of us; his observations show a high index of nigrescence in malignant disease. I think that point may be considered as established. Of course it does not necessarily follow that cancer is at all more prevalent among generally swarthy than among generally blond nations: nor am I aware of any evidence in favour of such a belief, though there may be a little against it. Thus the death-rate from it in Italy was in 1896 only 49·6 in 100,000; but it was increasing. And among Italians in America, in 1900, after allowance made for age, it was lower than in almost all other races. But the Scandinavians, who have an evil reputation in this respect in Europe, do not stand badly in America—better indeed than the English, Scotch, or Irish, and much better than the Germans. On the whole, there is some reason for supposing cancer to be a disease whose development is favoured by civilisation, comfort, and intellectual progress; and these are generally most prevalent in the races whom Huxley called Xanthochroi, although it is the swarthy individuals among them who suffer most.

John Beddoe.

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J. B.

ON THE LAWS OF INHERITANCE IN DISEASE

By JONATHAN HUTCHINSON, F.R.S.

WE all of us have had two parents, and with the rarest exceptions four grandparents. Most of us have had eight great-grandparents, and probably to a large majority no fewer than sixteen persons have stood in the relation of great-great-grandparents. Now since tendencies to individual peculiarities, involving, it may be, liability to special forms of disease, may be transmitted not only from parents and grandparents, but also from much more remote ancestors, it is obvious that their investigation presents us with very complicated problems. In many instances it is almost hopeless to seek to trace direct transmission from individual to individual, and we may arrive at safer conclusions by estimating average prevalence in races, families, or classes of society. It is in this latter way only that many questions which present themselves, not only to the physician, but to the biologist and to the student of sociology, can be satisfactorily looked at. Thus, in reference to such diseases as cancer and gout, we may reasonably suspect inheritance if we find them common in certain families or races, although it may often be difficult to prove direct descent from parent to child. [*Vide* art. on "Anthropology and Medicine."]

We must, however, at the outset endeavour to define approximately what we believe to be possible as to hereditary transmission. Without venturing to do more than mention the Weissman logomachy, which has recently disturbed the creeds of some biologists, I will take permission to avow my belief that with the sperm and germ supplied by parents there may pass to the offspring tendencies to the reproduction of everything that these parents had acquired up to the date of the sexual congress. By the term "acquired" is meant all that has been received by modification of vital processes, not what has been imposed or taken away by external violence. Not only, however, may offspring derive from parent cells peculiarities of cell and tissue structure with the proclivities attaching to them, but it is also in a high degree probable that in some instances parasitic elements or specific poisons may pass directly into the tissues of the embryo. Such parasitism may at the time be absolutely latent in the parent, and may remain so for indefinite periods in the offspring.

We have to deal, then, with the inheritance of structural peculiarities and tendencies which is more or less certain, and in addition to it with the possible inheritance of parasitic germs or of poisons, which is uncertain and in a sense accidental. Respecting this inheritance of specific poisons it is necessary here to premise that what takes place may be contamination *in utero* rather than inheritance in the more strict sense of the word. We limit the term inheritance to that which is derived from sperm or germ. The two parents do not stand in an exactly similar relation to their offspring in this matter. The father cannot possibly convey any poison unless it be present in the semen; the mother, on the other hand, is in vital relations with the fœtus for nine months after conception, and may, at any date during that period, convey to it any poison which has meanwhile found its way into her blood. Thus variola cannot possibly be conveyed by the father to the fœtus so as to develop only after the birth of the latter; but the mother may communicate it during any period of her pregnancy up to the last days. The same is the case with syphilis, and possibly with some other specific diseases.

It may be convenient to speak first of the laws of inheritance of those diseases which are caused by specific animal poisons. Of these the principal, and the one respecting which most is known, is syphilis; and it may be allowed to stand as an illustration of the rest. The facts in our possession make it very probable that when syphilis is derived by a child from a parent, it is conveyed by the actual transference of some specific material, probably of a particulate and organic nature. The child does not inherit any modification of tissues which the parent may have undergone, but takes over specific germs which are destined to multiply in its blood and produce phenomena of a similar character and in a similar order to those which its parent had previously manifested. This character and this order may be greatly modified, but they will be essentially the same. Thus, however much the health of a parent may have been damaged by syphilis, he will transmit to his offspring nothing unless the specific virus of the disease be present in his semen, and in those particular spermatozoa which go to the fertilisation of that particular ovum. A man might on this hypothesis beget a syphilitic child one week, and a non-infected one the next; nay, it is even possible that of twins one may receive the poison and the other escape it. It is necessary to state this definitely, for although we have as yet no direct proof of this proposition, the hypothesis is necessary to any clear comprehension of facts which are of every-day occurrence.

The hypothesis just suggested would lead to the expectation that the two sexes would be equally liable to suffer. There are, however, certain unexplained facts which seem to imply that from the effects of inherited taint girls suffer more frequently and more severely than boys. The proportions have been worked out chiefly in reference to the iritis of infants and the keratitis of more advanced life. In the former the proportion has been found by the writer to be 5 to 18, and in the latter 38 to 64; and Mr. Nettleship, in a recent report, has estimated it in 564 cases of

keratitis as 40 and 60 per cent respectively. The problem as to different incidence of inherited disease upon the two sexes presents itself in connexion with various forms of malady. Male children almost solely inherit the liability to bleed, and are also, it is believed, much more prone to display characteristic indications of gout early in life—before the influence of personal habits can have had much effect. As regards cancer, tuberculosis, leprosy, and many other maladies, the facts are too complicated to admit of any satisfactory conclusions as to the relative liability of the two sexes in connexion with inheritance. All the world over, with but few exceptions, leprosy is much more common in men than in women, but this has probably little or nothing to do with inheritance.

The following are the facts which appear to have been established respecting the inheritance of syphilis:—

That the father may infect his offspring (the mother having never suffered), and that this is by far the most frequent mode by which the disease is transmitted.

That the mother may infect her offspring, and that she may do this not only at the time of conception, but at any period during pregnancy, up to within the last few weeks.

That there is much uncertainty as to whether a child will or will not receive the poison of syphilis when born of parents one or both of whom are tainted. Thus a child may wholly escape under circumstances apparently full of risk.

That the nearer the conception to the date of the primary disease, in one or both parents, the greater the risk to the child.

That a parent in the tertiary stage may still suffer severely and yet have healthy offspring.

That the severity of the disease in the child is in no relation to that shown by the parent—many of the worst instances occurring in children of parents who were apparently in good health. Severity in the child is therefore probably, as in the adult, a matter of idiosyncrasy in the recipient, and not of peculiarity as to source.

Of twins one may suffer and the other escape.

Although it is the rule for those born soon after the parental acquisition to suffer and for younger ones to escape, yet now and then remarkable exceptions may occur.

That, with rare exceptions, the period during which a parent retains the poison of syphilis in a transmissible state is limited. In the father it rarely exceeds two years, but as regards the mother nothing trustworthy can be stated. The risk of transmission is probably of much longer duration in women than in men.

Although (unless we accept Schaudinn's spirochæte pallida) no one has yet recognised the specific microbe of syphilis, whilst in tuberculosis this has been accomplished, yet the facts respecting contagion and inheritance remain far more vague and uncertain in the latter than in the former malady. When a disease may be obtained by contagion unwittingly and very easily—its microbes being possibly almost omnipresent—it becomes

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very difficult to prove anything as to inheritance. Thus there are not wanting those who, relying too exclusively upon modern doctrines of bacillary causation, and supporting their creed by so-called statistics, are disposed to deny altogether the effect of inheritance in tuberculosis. In the investigation of this important question, we must not restrict ourselves to the narrow platform of tuberculous disease of the lungs. We must comprise all the various maladies with which we now associate the tubercle bacillus, and take in all forms of bone-, joint-, and gland-scrofula —also the various affections of the eye and the skin (lupus and its allies) which are in such association. If in this way we take cognisance of the whole domain of scrofula and tuberculosis, it is, I think, impossible for any one acquainted with the facts to disbelieve in the power of hereditary transmission, and to rest only on the theory of contagion from without. The subject is one much too complicated to be well suited for illustration by statistical calculations ; these are as likely to mislead as to help us.

Two factors are admittedly of great importance in reference to the development of tuberculous affections : we must take cognisance not only of the bacillus itself, but also of the state of the tissues upon which it is implanted. The possibilities of inheritance are therefore twofold. It may be that the bacillus itself may pass bodily or potentially with the sperm or germ from parent to child, or it may be that only a condition of tissues liable to its attacks, and prone to suffer severely under them, has been the result of transmission. If we are permitted to give an inclusive name to the tissue-condition which is prone to favour the development of the tubercle bacillus, that of "scrofula" will perhaps be convenient for the present. A child may then inherit "scrofula" without the bacillus, or the bacillus without "scrofula"; or, what probably is most common, both may be present together. Pathological facts leave us in no doubt that the tubercle bacillus may find its way into the body of the fœtus *in utero* and may there develop. Whether it does so in association with the semen, or in union with the maternal germ ; or whether it is always derived by the ovum from the mother's blood, we are as yet uninformed. We may plausibly conjecture that any one of these three modes is an easy possibility. The life-history of the tubercle bacillus is by no means fully known to us. We do not know, for instance, what are the conditions or how long the periods under and during which it may remain latent in the tissues. Many clinical facts suggest that it may in some resting form be present in most persons— waiting until some local damage or some degradation of general health gives it opportunity for development. The prevailing creed which suspects external contagion as the cause of all scrofulous and tuberculous attacks is probably a much too narrow one. It is clear, however, that as regards the heredity of pulmonary tuberculosis and scrofula, we can at present do little more than state preliminary facts and suggest possibilities. We are by no means yet in a position to put forward conclusions.

If we turn from tuberculosis to leprosy, a malady which is possibly a congener, we shall encounter similar sources of uncertainty. Yet, if

we can get a clear view of the facts, the two will perhaps throw some light on each other. A bacillus very like that of tuberculosis attends the development of all the more severe forms of leprosy. When leprosy ends fatally, it is often by the supervention of pulmonary disease not distinguishable from pulmonary tuberculosis. The facts as regards contagion are much the same in the two, and are matters chiefly of conjecture. In both maladies it is certain that almost unlimited opportunities for contagion may occur without any evidence of its accomplishment. Now, until quite recent times, the belief in the hereditary transmission of leprosy has been almost universal. The more careful investigations of modern observers have, however, thrown much doubt upon this creed. It is quite certain that the children of lepers, born out of leper districts—in England or the United States for example,—never inherit it. The occurrence of the disease in the children of lepers in a leprosy district is no evidence at all; for obviously they have been exposed to the endemic cause, whatever that may be. If it be, after all, a food disease, they may have partaken of the tainted substance. The inquiries of the Leprosy Commission in India, which collected facts at the Schools for the Children of Lepers, pointed to the conclusion that there is no proof of heredity, since these children did not manifest the disease in greater proportion than others. The very prolonged periods during which leprosy may remain absolutely latent (ten years or more) introduces, however, an element of uncertainty into all these investigations. We may safely believe that in the case of leprosy the influence of heredity is a very small factor, but it would be unwise to deny its possibility. The suggestion that it may be communicated to infants by the mother's milk, or by food contaminated by leprous hands, may be allowed to explain all the facts which have hitherto been supposed to prove inheritance.

If we turn now to the consideration of maladies which are induced, neither by any specific virus nor any parasitic microbe, but by the inheritance of anatomical or physiological peculiarities, a few general propositions may be ventured.

There is probably no peculiarity, whether of structure, of function, or of both, capable of being acquired or augmented during the life of the individual which may not be reproduced in his or her offspring; yet the transmission of such peculiarities is by no means a matter of certainty: one child may suffer and another escape. Of this uncertainty double parentage is no doubt the chief explanation.

It is quite possible for an individual in whom any given tendency derived from a parent may never have disclosed itself to transmit such tendency. Thus a disorder or peculiarity present in a grandfather may be revealed in his grandchild, just as special features in the countenance or other resemblances may be transmitted. It is possible, indeed, that a peculiarity of structure leading to derangement of function may be transmitted through many generations, and yet show itself in very few individuals in each. Under some law, as yet not well understood, it is possible

for a peculiarity of structure to show itself suddenly in several children of the same parents, there being no proof of its previous occurrence in the progenitors. To this last group of maladies the term "family diseases" has been given; but it must be clearly understood that it refers to the members of one single family and not to descendants in several generations.

Illustrations of the wide topic upon which we now enter occur on every side. The inability to digest the albumin of eggs and of milk, which is often met with as an idiosyncrasy in related individuals in several generations, must depend upon the constitution of the gastric juice, which in its turn is due to some peculiarity in the glandular apparatus of the stomach. It may serve as an example of a thousand other peculiarities, some more and some less well marked. To the whole group we give the name idiosyncrasies; and although we leave them for the most part unexplained, they are none the less real, and dependent, no doubt, upon actual structural aberrations. Very often a sufferer knows that some predecessor—grandparent or great-grand-parent—had the same peculiarity. Were habits of family observation and record more cultivated, no doubt such evidence would be still more frequently forthcoming. Every idiosyncrasy that can be named has doubtless its physical basis, and is liable to be transmitted in inheritance.

Cancer.—As regards the heredity or otherwise of cancer, statistical compilers are somewhat at variance with those who are content to base their beliefs upon personal impressions. With one accord the latter declare that not only is the tendency to cancer often inherited, but that heredity is one of the commonest of its causes. Those who have attempted to test the question by appeal to figures have, however, usually arrived at a different conclusion. It may be suggested in explanation that the methods adopted were not likely to give satisfactory results; a few off-hand questions put hurriedly to the patient are not adequate, and the potent influence of atavism must also not be neglected. All that the so-called "statistics" on this question have proved, is that in a large number of cases of cancer its subjects are either not aware or are not willing to admit that any near relative has previously suffered from the disease. Such negative evidence cannot, in the minds of those enjoying opportunities and accustomed to make minute inquiries, explain the facts which confront them day by day. They see so frequently instances of a number of relatives becoming in turn the subjects of cancer, that the conviction is forced upon them that something of the nature of inheritance must be at the root of the matter. Their impressions are confirmed by the observation that in cases in which young persons are the sufferers there is almost always a family history. It is further very difficult, without having recourse to heredity, to explain the varying prevalence of cancer—the different countries and communities, and its comparative absence in primitive races and amongst wild animals. It must be supposed, in explanation of the heredity of cancer, that what is transmitted is not any germinal matter or plasma, but a tissue proclivity which renders the

individual more prone than others to originate in adult structures the fœtal modes of cell-proliferations which are its chief characteristic. If we may admit that it is probable almost to certainty that this proclivity exists in greater force in some individuals than in others, we have next to ask what the influences which tend to evoke its activity are. Amongst these it seems probable that local irritation or direct injury stands first, and that the early stages of senility, whether of the individual or the organ, are those in which the vulnerability is at its height. The recently proved fact that the introduction of arsenic into the system is powerfully influential in increasing the proclivity, and may cause the production of various forms of malignant growth at the same time in the same hereditarily predisposed person, is one the bearings of which are perhaps not yet fully perceived.

The laws of inheritance come to our aid in explanation of many of the peculiarities presented by exceptional diseases of the skin; and these in turn illustrate the laws of inheritance in a very instructive manner. Inherited peculiarities in structure must be invoked to explain such a phenomena as excessive tendency to freckle; the liability to blister in the sun, proneness to chilblains, liability to urticaria and pruritus. It is for the most part those who have inherited a skin in which the sebaceous glands are large who become the subjects of comedinous acne.

Psoriasis does not very often affect several brothers and sisters, but it frequently seems to be transmitted from parent or grandparent. Thus it may persist through many generations, but still affect but very few individuals. Its subjects are almost always in good health, and the balance of evidence as to its nature would incline us to suspect that it depends upon an inherited peculiarity of the structure of the skin.

Amongst the "family diseases" which chiefly show themselves on the skin we have the common forms of xerodermia or ichthyosis; and the rare malady known as Kaposi's disease, or xerodermia pigmentosa. In ichthyosis almost invariably one-half of the family of children suffer whilst the others wholly escape. Evidence of it is often but not always present at birth. There appears to be no regard to sex. The same statements are true of Kaposi's malady, better known, perhaps, as "Lentigo maligna juvenilis," which consists of a most excessive tendency to the formation of freckles, which are apt to run into ulceration and finally into cancer. Its occurrence reveals a congenital imperfection in the structure of the skin, which renders it unable to withstand the irritation of ordinary sunlight. In this feature it has much in common with retinitis pigmentosa, a disease occurring often in several members of one family, and due to degenerative changes in the retina apparently induced by exposure to light.

The tendency to bleed on slight cause, which constitutes the "hæmorrhagic diathesis," affords us another good example of a family disease. It is, however, not one of those which is restricted to a single generation, being almost always an heirloom, and with the peculiarity that it manifests itself almost exclusively in the male sex. It is quite

possible that our inferences on this latter point may be somewhat exaggerated, for the menstrual relief in women not improbably prevents other forms of hæmorrhage, and in families in which the males are bleeders menstruation in the women is often profuse.

The proved relationship of hæmophilia to inherited gout leads to the consideration of the latter malady itself in reference to inheritance. This is a topic which requires much patient attention to detail for its clear apprehension. It is not a simple matter: we must not restrict our conception of gout to attacks of acute podagra, but must include in the term all the conditions which lead up to such attacks, or can be proved to be in association with them and with the same class of causes. By general consent the liability to gout is hereditary; indeed, it may even be doubted whether in its more typical forms it is ever acquired in a single generation. That the gouty state may be induced by luxurious living and defective exercise, is a proposition which no one will deny; that it can be so induced with equal facility in all persons, is, however, well known not to be the case. In some, very slight errors in self-management will cause it; whilst in others no excess, however long continued, seems to be efficient. The difference, as we observe it under the existing conditions of society, is probably in the main a difference in the strength of inheritance, though at the same time it may be true that certain differences in race, family, and temperament may in the first instance have made themselves felt. Of the middle classes of society in England, and amongst other communities where gout has been long prevalent, it may be held that all inherit the tendency more or less definitely. If we attempt to explain in what that tendency consists, we must begin by saying that in the first place it depends upon peculiarities of appetite and digestion, and next upon defects in the excretory organs. The man who inherits gout inherits peculiarities of stomach and kidneys, and of all the organs which are concerned in the assimilation of food and the depuration of the blood. We may take this as perhaps the simplest expression of the inheritance of gout; but there must follow on it the assertion that he inherits also peculiarities of various other kinds. His cartilages and ligaments, his nerves, his muscles, his blood-vessels, in fact every tissue in his body, has acquired some modification, and with it some special proclivity in reference to disease. Congestions, inflammations, nerve-pains, whatever may have been their exciting causes, will in him assume a special character and lead to specialised results. Thus the offspring of generations of gouty ancestry may, in virtue of such descent, suffer from various maladies which stand in no direct relation with errors in diet, defective assimilation, or the accumulation of urates in the blood. One of these is the weakening of blood-vessels, which is the proximate cause of hæmophilia, and may also find its expression in epistaxis, hæmorrhagic purpura, menorrhagia, bleeding into the vitreous, and other phenomena. In the same way inherited gout may be the parent of iritis in early life, and of various forms of joint disease at all periods of life: many of them are wholly unassociated with the deposit of urate of soda

in the structures. It is an inheritance of tissue proclivity independently of, though usually in addition to, peculiarities of assimilation and excretion. Nor must it be forgotten that these inherited liabilities may have been inextricably mixed with others. Feebleness of circulation, instability of nerve function, scrofula, and other causes of disease, may have joined with inheritance of gout, and the resulting states may thus become very complicated.

It is not necessary to say more than a few words respecting the heredity of congenital defects in the growth of *external parts.* It is universally admitted that such defects as coloboma iridis, hare-lip, superfluous digits, webbed digits, and the like, may be and commonly are hereditary. We also observe respecting them that occasionally they occur in many members of the same family; whilst there is little or no evidence as to their occurrence in former generations. This has been especially noted in certain instances of hare-lip and defects in the iris, and it is especially of interest in reference to the explanation of other forms of "family disease."

A curious group of congenital affections in which, no doubt, the influence of parentage should be traced, is constituted by those which show that the two halves of the body are not exactly alike. In some of these the proofs are conspicuous at birth, but in others they only become manifest on the occurrence of some disease which affects the limbs, etc., of one side more severely than those of the other. Slight manifestations of this kind are very common and should be carefully allowed for by the clinical investigator, since they may mislead him in his inferences as to bilateral symmetry. Very definite examples of congenital difference are common in the occurrence of a myopic eye on one side and a normal or hypermetropic one on the other, and amongst the more exceptional ones are hemi-hypertrophies of the skull and other bones, and the unilateral development of nævoid conditions of the skin. Of this latter portraits may be found in the Museum of the Hôpital St. Louis and the London Polyclinic.

The influence of the age attained by parents at the date of procreation may be reasonably supposed to be in some degree influential on offspring. In some instances a parent may have acquired immunity as regards certain specific diseases, such as measles, small-pox, and syphilis, and may transmit some immunity in a certain degree of reduced susceptibility to his offspring. It is probably in this way that we must explain the well-established fact that communities in which these maladies have prevailed for many generations become less liable to suffer severely from their attacks than are virgin populations. The opposite is probably the fact as regards certain other heritable tendencies, such as that of gout. In perhaps a majority of instances an inherited liability to gout becomes strengthened by personal habits, and an old man may be supposed to be much more liable to transmit it than he was when young. Is it the fact that the younger members of large families more often show tendency to the affections which are in connexion with gout than do the elders? Some observers have thought that this is really so. It has

even been further suggested that the children of aged parents are much more liable to cancer than the children of the young. If such is the case the inheritance is probably of tissue proclivity only. A yet more subtle form of inheritance in connexion with age of parent has been suggested in reference to the nervous system. Certain facts have been quoted which are supposed to show that remarkable precocity of intellect and some exceptional ability are manifested in the children of aged fathers. The instance of the great Chinese philosopher, Confucius, whose father was seventy at the time of his birth, must suffice to illustrate what is meant.

A most interesting and instructive example of the length of time which may elapse before the effects of pathogenic inheritance are realised is afforded by what is well known to occur in interstitial or parenchymatous keratitis. An infant is born of syphilitic parentage and suffers from the usual symptoms during the early months of its life. After recovery from these a period of absolute immunity occurs, which may extend over many years. At the age, it may be, of ten, twenty, or even thirty years, the eyes inflame and pass through a very peculiar and often very severe attack, which is destined after a time to pass away spontaneously, and which in a well-marked form never occurs again. Usually the two eyes suffer simultaneously, but if exceptionally only one is attacked the other will probably follow after the lapse, it may be, of several years. The cornea is the structure principally affected, but it is by no means exclusively so, for the iris and the choroid often suffer also. At the time of the occurrence of the keratitis there is no reason to suspect any blood change, nor can any exciting causes for the attack be detected. It seems unquestionable that the tissues of the eyeballs were from infancy, in virtue of the inherited taint, destined to inflame, and the problem before us is to explain the prolonged delayal of the attack. Nothing has ever occurred in connexion with these cases (common enough) to suggest the patients' fluids were still a source of danger as to the contagion of syphilis, and with the exception of articular affections (probably resulting from infection from the eyes), no other specific phenomena attend the attack. In a few instances the patient had attained the age of forty before the inherited attack of keratitis occurred.

The lesson which is here so definitely conveyed may probably be extended over a wide clinical field. In gout it is well known that many special forms of local disease in connexion with the inherited predisposition, and little if at all connected with personal habits, appear to wait for their development until a certain age has been attained.

It is exceedingly important to remember, as just stated (see above), when we endeavour to apply our knowledge of the forces of inheritance to the elucidation of the phenomena of disease, that the inheritance is often multiform. We but rarely encounter cases in which a strong inheritance exists in one definite direction and in that alone. Thus the taint of parental syphilis may occur in a child who also inherits gout or scrofula, and an inherited tendency to liver disturbance by no means excludes definite

proclivities in other directions. Thus maladies which may receive distinctive names, as if they were well specialised and almost *sui specici*, may after all be only the hybrid or partnership results of several efficient inherited tendencies which have become combined. In such cases the procedure should be one of pathogenic analysis, and endeavour should be made to resolve the product into its component elements. The disease known as Hebra's sarcoma melanodes supplies an example of what is meant. This affection, which has recently attracted much attention, may be assumed to be in the main a consequence of inherited gout. In the form in which it is seen in children or young persons, there is probably also inheritance of tissues prone to chilblains. In the senile form the causes are more complicated, and the lithæmia of acquired gout reinforces the inheritance and combines with the liability to malignant neoplasms which belongs to advancing years, and which may also probably be inherited. The disease is by no means simply a form of gout, still less is it in any close relation with typical forms of melanotic sarcoma. It partakes, however, of the essential nature of both, and that in virtue probably of the double inheritance. If we are allowed to suggest that its subjects not improbably inherit at the same time a tendency to psoriasis or its modification lichen planus, the epithet multiform will be seen to be yet more definitely applicable.

Another important law which receives occasional illustration in these very obvious hereditary defects is that of "transmutation in transmission." By this expression is meant that the defect reproduced is not always exactly the same as that in the predecessor. Thus one child may have a superfluous digit, and another of the same family merely a deformed and overgrown one. When coloboma of the iris occurs in a family there are almost always some in whom there is no cleft, but only a patch of colour marking the site of the cleft in others. Mr. Clement Lucas has recently drawn attention to the fact that one or other of the parents of hare-lip children has often a defective formation of the gum at the junction of the premaxilla although no trace of cleft in the lip. *Nemo fuit repente turpissimus* seems as applicable in reference to disease as it is to moral character, and it applies with special force to the tendencies which are inherited. What is hereditary is clearly a liability to disturbance in the development of a certain portion of protoplasm, but may fall short of the necessary production of identity of result. This law is probably of wide application under conditions in which it is not so easy to prove its influence. In the case of various forms of skin disease it may be conjectured that a liability to defective formation of the skin in general is the antecedent rather than a definite proclivity to one single type of malady. Thus an inheritance from a parent who has suffered from psoriasis may possibly be transmitted as ichthyosis, or some form of chronic eczema or lichen. Many of the known facts as regards "family diseases" support the belief that some law of "unity in variety" influences their production.

JONATHAN HUTCHINSON.

MEDICAL GEOGRAPHY

By F. G. Clemow, M.D., D.P.H.

History of Medical Geography as a Science.—From the earliest times mankind must have observed that diseases were not quite evenly distributed over the earth's surface. Localities, even in primitive ages, must have gained reputations for healthiness or unhealthiness; and this is but another way of saying that all or many diseases, or perhaps one particular disease, were observed to be rare or absent in some places, frequent and severe in others.

Hippocrates, in the limited portion of the earth's surface known to him, recognised clearly the influence of geographical conditions upon disease prevalence; and so, to a less extent, did the later Greek, Roman, and Arabian medical writers. But for many ages these observations remained a series of isolated facts, bearing but little relation to each other, and apparently throwing but little light upon any particular problem in medicine. It remained for later times to attempt a world-wide survey of the distribution of each disease, and, after collecting observations from all portions of the terrestrial globe, to arrange them systematically, and thus be in a position to draw conclusions, based on those premises, as to the natural history of the disease in question. As a science, therefore, Medical Geography is of comparatively modern growth. The reason is not far to seek. Until quite recently materials for a world-wide survey of any disease did not exist. Immense areas remained unexplored and almost unknown; and countries that were known and explored were rarely seen by skilled medical observers, or if seen, were rarely reported on at length. But fortunately, within recent years, a great improvement in this respect has taken place. Colonial expansion, commercial enterprise, missionary zeal, exploration for the mere love of exploration, or of sport, or for some general or special scientific object—have all perhaps been factors in opening up to our knowledge the formerly unknown or little-known regions of the world. To these must be added the enormously increased facility of travel, the extension of education among the masses, and the improved means of cheap publication, whereby books and articles upon the results of travel and exploration are now brought to the hands of thousands who in former times would scarcely have known that such expeditions had taken place. The result has been a great awakening of interest on all sides, and in all classes, in everything connected with newly-opened-up countries. Moreover, this interest has not been confined to the utilitarian or picturesque aspect of those countries, but has embraced—recently in quite a special degree—the medical and sanitary problems which those regions present. The increased interest in these problems, both within

and without the ranks of the medical profession, has been stimulated, not only by the general causes just mentioned, but also by certain special causes, which should be mentioned here, as many of them form important stages in the history of medical geography as a science. Among these causes the most prominent place must be given to the increased knowledge recently gained of the causation and mode of spread of diseases in general, and of so-called "tropical" diseases in particular.

The magnitude of the discovery that many—probably all—infective-disease processes are caused by minute living organisms can hardly be over-rated. Scarcely second to this in importance has been the proof, within the last decade, that malaria is caused by a blood parasite, and is spread by the bites of mosquitoes. An immediate application of the lesson taught by this discovery has already led to the effective control of malaria in many places where it was formerly uncontrollable. The economic and the moral results of this discovery and its application are perhaps incalculable. The sense of helplessness in the presence of a disease, the cause of which appeared to elude detection, and the ravages of which seemed to be to a great extent beyond human control, should now disappear. Regions hitherto regarded as all but uninhabitable may yet be opened up to man's labour and profit; and in cities and towns where malaria prevails, the enormous economic loss from lowered vitality, actual sickness, and death, if it does not disappear, should at least be much diminished.

The great pandemic of influenza in 1889-90; the sudden revival in 1894 of plague in the Far East—a disease which up to that date had seemed to be almost as extinct as the sweating sickness of the Middle Ages; its recent serious spread in India; the demonstration that yellow fever is carried by mosquitoes, and may therefore be controlled by suitable measures; the wide extension of sleeping sickness in Africa, and the discovery (now almost complete) of its cause—these and other incidents have all served to arrest the attention of the public, the medical profession, and the administrative authorities. Governments have awakened to a fresh sense of responsibility, and to a recognition of the vast importance of studying these and all other diseases, and of equipping their colonies, armies, and navies with the means both of studying and controlling them. Schools of Tropical Medicine have been opened; universities have instituted diplomas of Public Health and Tropical Medicine, to obtain which a full knowledge of this branch of medicine is essential; no Congress of Medicine is complete without a section devoted to this subject; and journals now exist in all the principal languages dealing with its study alone. Great Britain has been the pioneer in all these advances, and to British observers some of the most striking of the discoveries alluded to above are due. To this result the scientific expeditions to tropical regions, despatched by the Royal Society and other bodies, have largely contributed.

Statistics as the Basis of Medical Geography.—While the materials for a world-wide study of disease distribution are, as already stated,

incomparably more abundant than they were formerly, they are still very far from complete. The relative frequency of any disease in different portions of the earth's surface can be accurately gauged only by a study of statistics; and it is almost a truism to say that, if they are to have any value, such statistics must be both complete and accurate. They should, moreover, deal with *cases* of the disease rather than with *deaths* from it. Unfortunately, from very large areas of the globe, no statistics at all are forthcoming. From others mortality statistics of some kind are available, but they are neither complete nor, there is reason to believe, wholly accurate. In others, again—as in some of the principal European countries—statistics of greater trustworthiness are published, though they are often lacking in completeness. So far as my observations have gone, it would appear that the most reliable and complete statistics of disease as a cause of death published in any country are those issued by the Registrars-General for England, Scotland, and Ireland. But statistics of disease as a cause of sickness are still more rarely available, and, when available, are for obvious reasons still less trustworthy, than statistics of disease as a cause of death. The ideal of complete and accurate returns of all cases of disease, from all portions of the earth's surface, is, and perhaps must ever be, an unattainable one; in the meantime the medical geographer can only cite mortality statistics for certain countries—with a warning that they have but a relative value; and, for other countries, must fall back on such statements as that a disease is "frequent," or "rare," or "exists," or some similar general assertion.

Two methods of grouping the subject matter.—In text-books upon medical geography—of which a considerable number have now been published in English, French, German, and other languages—the subject-matter is usually grouped in one of two ways:—in the first, the various countries or other geographical divisions of the globe are taken as the heads of chapters or sections, and under each of these heads statements are made as to the behaviour of the principal diseases observed there; in the second, each disease is considered separately; its behaviour is traced from country to country, and from one continent to another; and in this manner the material is made readily available for conclusions on the relation of the particular disease to geographical conditions. Each of these methods has its advocates. The first method presents the facts in a form useful for persons about to visit any country, and wishing to know something of the diseases likely to be met with there; but it has the disadvantage that, unless supplemented by a summary of the facts arranged according to the second method, it serves to throw no light upon the natural history of the disease dealt with. Since the primary aim of medical geography is to supplement clinical and pathological facts with geographical facts, and in the light of the latter to endeavour to solve some of the problems of disease causation and prevention, it would seem that the second of the above two methods is the only truly scientific one to be adopted in treatises dealing with this subject. A single example will illustrate the truth of this contention.

The statements that in the Straits Settlements scarlet fever is unknown, enteric fever rather common, and beri-beri exceedingly so, are statements of isolated truths which are without relation to each other, and which contribute nothing to our knowledge of any of these diseases. But the statements that scarlet fever is unknown in the Straits Settlements, that it exists but is rare in Southern China, and that it is far less uncommon in Northern China, are statements of closely related association, which, when corroborated by similar facts in other longitudes and in both hemispheres, justify certain definite conclusions as to the relation of this disease to latitude, climate, and temperature.

Necessity for treating the subject historically.—A study of medical geography is not complete—and may indeed be misleading—unless supplemented by a study of medical history. Hardly any disease has a permanent geographical distribution. Even those diseases which are practically ubiquitous vary from time to time in their virulence and in the number of their victims. But it is particularly in the large class of "epidemic" disorders that a study of their history becomes of the greatest interest and value. Materials for such a study are even less complete and trustworthy than those for a study of their contemporary distribution. The scanty records of disease prevalence in the earlier centuries, the loose medical phraseology too often found in them, the consequent uncertainty as to the nature of the epidemics when they are mentioned, the complete absence of records from many countries, and the resulting vast gaps in the history of any given epidemic—are some of the difficulties which confront the historian of disease. Attempts have, from time to time, been made to put in tabular form the chronicles of epidemic diseases; and much valuable material of this kind is found in the pages of Noah Webster, Schnurrer, Hecker, Haeser, Hirsch, Theophilus Thompson, and others. But the incompleteness of such records is all too obvious; and when it is recalled that, even in the case of the Black Death of the fourteenth century—the most appalling epidemic phenomenon in all history, which caused in Europe the death of perhaps one out of every four persons then living,—the source of the disease is still unknown and a matter of controversy, it will readily be understood how difficult it is to trace the history of other less striking disorders. But, incomplete as the historical records are, they throw valuable light upon the problems of medical geography. They show how all diseases have waxed and waned from century to century, or from year to year; how some—such as the sweating sickness and leprosy—have wholly or partly disappeared from countries where they were formerly common; while others, such as cholera, have appeared in the West only in comparatively recent times. But perhaps the most important lesson they teach is the need for great caution, lest sweeping conclusions should be drawn as to the distribution of any disease from knowledge of its behaviour through too short an historical period. No more striking example of this danger could be found than in the recent history of plague. Until the year 1898 this disease had never been observed south of the equator, or in the

western hemisphere; and writers upon plague seemed justified in asserting that the infection could not spread to the New World or to southern latitudes. Yet its recent epidemic appearance in Australia, South Africa, North and South America, and elsewhere has shown how fallacious was this view. Scarcely less striking examples have been the recent spread, for the first time in history, of the chigo disease across Africa to Madagascar and India; and the wide diffusion of sleeping sickness to areas where it had, so far as is known, never been seen before. It would be easy indeed to multiply examples. Malaria appeared for the first time in Mauritius about the year 1866; syphilis, tuberculosis, measles, and many other diseases are constantly being introduced to races and tribes free from them until brought into contact with the ever-widening stream of civilisation; ankylostomiasis was recognised in England for the first time in 1903; and, in brief, every year—almost every month—brings some observation of a like character.

Forces which determine the distribution of disease. — The distribution of any disease must be looked upon as the resultant of a large number of forces; and it is the function of medical geography to determine, for each disease, what those forces are and how they act. Certain of these forces may be regarded as intrinsic to the disease itself, and associated with its etiology and mode of spread; others may be regarded as extrinsic, or more purely geographical forces—such as nearness to or distance from the equator, altitude above sea-level, temperature, humidity, nature of the soil, racial influences, and the like. Each of these variables will be dealt with separately in a later part of this article; but it will be convenient first to consider the intrinsic forces connected with the etiology and mode of spread of the disease itself.

(A) *Forces inherent in the disease itself.*—For the purposes of medical geography, diseases may most conveniently be divided into those which are caused by the action of parasites and those which are not. The word parasite, as here used, includes not only the macroparasites, such as the guinea-worm, the intestinal "worms," and the like, but also the microparasites, such as the bacilli, cocci, amœbæ, hæmatozoa, and trypanosomes, which are the proved or suspected causes of the vast group of "infective" diseases. This division into parasitic and non-parasitic diseases is important from a geographical point of view, because in the former the factors concerned in the geographical distribution act in a manner different from, and more complex than, in the latter. Thus in the case of a disease not of parasitic origin, the geographical forces mentioned above must be supposed to act only or mainly upon the individuals suffering from the disease. But in the case of a parasitic disease it is clear that these forces may act, not only on the individuals who are the human hosts of the parasites, but also upon the parasite itself.

The parasitic group of diseases may further be divided, for geographical purposes, into two sub-groups: those in which the parasite must spend part of its life-history in an extra-human host, and those

in which the parasite is not known or even believed to require any such extra-human host. To the first sub-group would belong the various filariases, malaria, and yellow fever, in all of which a mosquito is essential to the life-history of the parasite; the guinea-worm disease, in which the parasite requires a certain fresh-water cyclops to complete its life-cycle; sleeping sickness, which appears to be associated in the same way with the tsetse fly; trichinosis, associated with the pig; hydatids, with the dog and other animals; and the affections caused by tænia solium, tænia mediocanellata, and bothriocephalus latus, which require respectively the pig, bovines, or fish for the extra-human phase of the associated parasite. To the second sub-group would belong the large majority of the infective disorders, proved or believed to be caused by micro-organisms which seem to spend all or most of their life in the tissues of a human being, and to pass from one person to another without any intermediate host. It is clear that in this sub-group the geographical forces mentioned above will act only on the human host and the parasite, while in the former they will act not only on the human host and the parasite, but also on the extra-human host. This third factor will often, indeed, prove to be the determining element in the distribution of such diseases. A single example will suffice to show the truth of this statement: the absence or rarity of yellow fever in high altitudes is almost certainly due, not so much to the effect of the altitude and all that it implies upon the human subject or the parasite of the disease, as to its effect upon the mosquito host, which cannot live there; and the absence or rarity of the mosquito determines the absence or rarity of the disease.

In the case of those human disease parasites which do not require another animal host to complete their life-cycle, much remains to be learnt as to their behaviour outside the human body. In regard to many—such as the hypothetical parasites of measles, typhus, syphilis, and the like—it would seem that they have only the briefest, if any, extra-corporeal existence. They seem to pass directly from person to person, and in the absence of susceptible subjects they die out. Such parasites, if they exist, are never exposed directly to geographical influences; they can only be affected indirectly by the action which such influences exert on their human host. The various prevalence from time to time of such diseases must be attributed partly to varying degrees of activity or virulence of the parasite, partly to varying degrees of resisting power in the tissues of the persons exposed to them.

In the case of other diseases the parasite seems to be capable of spending a longer or shorter extra-corporeal existence in some medium known or unknown. Of the known media may be mentioned the bodies of other animals, water, air, the soil, the artificial media of the laboratory, and "fomites." Each of these media may play its part in the diffusion of the disease over the earth's surface—either for short distances, thus determining what may be called its "topographical" distribution, or for long distances, thus determining its "geographical" distribution. Each may be briefly considered separately.

The parasites of many diseases may and do occur in the *bodies of other animals.* These parasites must be distinguished from those mentioned above, which must enter the tissues of another animal to complete their life-cycle. Apparently they can pass from animal to animal or from animal to man, as they can also pass from man to man or from man to animal. Some, as, for example, glanders, farcy, hydrophobia, anthrax, and foot-and-mouth disease, are, indeed, essentially animal diseases, and only affect man occasionally. Others are essentially human diseases, but occasionally affect animals. To this group would belong the parasite of plague, which may attack rats, mice, monkeys, squirrels, bandicoots, cats, and other animals; that of influenza, which attacks horses and other domestic animals; that of scarlet fever, which appears to be capable of affecting bovines; and that of human tuberculosis, which in all probability —though the matter is still *sub judice*—is identical with the parasite of tuberculosis in cattle. It is clear that, for each of the diseases named, the movements and the distribution of the associated animal may have much to do in determining the distribution of the disease. It should further be noted that in many instances the lower animals may be passive transmitters of a disease, without themselves suffering from it. In this respect much suspicion has recently attached to insects such as bugs, fleas, lice, and ticks, which may suck the blood of an infected person or animal and immediately after bite a healthy person or animal, with obvious risk of transmitting the disease. This is thought by some observers to be one of the principal means by which plague is spread. It is certain that flies and other insects which may settle on an infected person or his excreta may carry away some of the infecting material clinging to them; and may thus be the means of spreading the infection.

The principal parasites of human disease, which can exist in and be spread by means of *water*, are those of cholera, enteric fever, and dysentery. Cholera has in many instances been diffused in towns and villages by a contaminated water-supply; and there is reason to believe that the virus has on some occasions been carried over long distances by infected streams, or even by such large rivers as the Hooghli, the Volga, the Thames, the Elbe, the Don, and others. Enteric fever and dysentery are probably spread over shorter distances by the same means. Indirectly, moreover, water is essential for the prevalence of malaria, yellow fever, bilharziosis, guinea-worm disease, ankylostomiasis probably, and others, since the extra-human hosts in which the parasites of these affections spend part of their life-cycle live in water during a part or the whole of their existence.

The period during which human disease parasites can live in the *air* is probably, for most disorders, a brief one. If disease germs escape from the body of a patient into the air, they are probably soon killed, or rendered innocuous, by the effect of light-rays, of desiccation, and of oxidation. The air immediately surrounding a person ill with typhus fever, scarlatina, small-pox, and similar diseases seems to be constantly

charged with the germs, whose numbers probably diminish rapidly as distance from the patient increases. In small-pox, however, there is proof that the germ may be carried over distances to be measured in fractions of a mile. It is probable that the air acts in spreading such diseases only by carrying infected dust-particles. In the case of small-pox, ophthalmia, and perhaps enteric fever and other diseases, these dust-particles are probably fragments of dried discharges from persons suffering from the disease. The air can scarcely be regarded as an important medium for the spread of diseases over long geographical distances—as from country to country, or from continent to continent; though, as a carrier of mosquitoes or other insects infected with disease germs, it is conceivable that the air may have occasionally acted in this way.

Many pathogenetic parasites can spend a longer or shorter period in the *soil.* The tetanus bacillus seems to occur widely in the soil; the parasites of malignant œdema, anthrax, mycetoma, actinomycosis, and others, can probably live for considerable periods in or on the earth; and it is possible that the same holds good for the parasites of enteric fever, plague, and some other diseases. The chigo-flea inhabits dry sandy soils, or the earthen floors of native huts; the ankylostoma may also occur in moist earth, and pass thence to man's tissues, either by penetrating the skin or by being swallowed with earth-soiled food, or through the practice of geophagy. The carriage of soil infected by some of these diseases may occasionally be a means of diffusing the disorder, but it can scarcely be regarded as an important one; and the suggestion formerly made that disease might be spread by the germ growing in the soil from a centre, as a patch of ringworm spreads, finds little to support it in the way of observed facts.

The *artificial media of the laboratory*, as a nidus for disease germs outside the human body, need not be dwelt upon at length, but they constitute the final proof that the parasites of some human diseases can exist for long periods outside the body of a person suffering from the disease, provided that the conditions are favourable. Moreover, in more than one instance—as, for example, in the small outbreaks of plague in Vienna and on an island near St. Petersburg—human disease has thus been introduced to a locality where it did not exist before, though fortunately in circumstances which permitted its immediate abatement.

It has long been believed that many disease germs may live for lengthened periods outside the human body, attached to clothing, rags, furniture, bedding, grain or other food-stuffs, or any other of the objects which are usually spoken of as "*fomites.*" Laboratory experiments have confirmed this belief in regard to many diseases. Next to the movements of infected human beings, the movements of infected fomites must be regarded as the most important factor in the spread of communicable diseases over long distances. Nor should it be forgotten that, in many instances where a disease has appeared to be spread by the movements of a human being, the infecting material was really carried

in his clothes or belongings, and not in his body. This must always[1] be the case when the person in question has not himself been attacked by the disease; or when he has travelled from the source of infection over a distance which takes longer to traverse than the incubation period of the disease. The length of time during which pathogenetic germs can retain their vitality when attached to fomites varies widely with the nature of the germ, the character of the object to which it is attached, and the presence or absence of favourable conditions of temperature, moisture, light, and the like. In scarlet fever, cases have been recorded which seem to show that this period may be one of many months, or even a year or more; in plague it may possibly be of such length as to enable the infected object to be carried over many thousands of miles, and even from one hemisphere to another.

In the above paragraphs diseases of parasitic origin only have been considered. They are of the greatest interest to the medical geographer, as they are communicable, either directly or indirectly, from person to person, and are associated with a definite, tangible something, which, though essential to the disease, is not the disease, which can be carried from one place to another, and whose distribution over the earth's surface is in many ways analogous with the distribution of other living objects—animal or vegetable. It is, perhaps, important to emphasise the truth that a parasite, though essential to the disease, is not the disease itself, nor has it of necessity exactly the same distribution as the disease. It suffices, in proof of this, to urge, first, that the parasites of malaria, filariasis, cholera, hydatids, trichinosis, and perhaps enteric and many other diseases, may exist outside the human body for long periods, in one of the natural media named above; and may therefore have a wider distribution at any moment than the corresponding disease; and, secondly, the existence, in laboratory test-tubes, in most of the principal towns of civilised countries, of the parasites of all the leading infective disorders, although, in regard to many of them, cases of the disorder itself may not exist within a thousand miles. Nor, for reasons which I have developed at some length in my recently published book, *The Geography of Disease*, is the distribution of a disease quite comparable with that of a plant or animal, though the distribution of a morbid parasite has, as just stated, much in common with that of the other kindred forms of the animal or vegetable creation.

In the case of diseases not of parasitic origin, the factors which determine their geographical distribution vary with the nature and causation of each disease. Some, as for example ergotism and pellagra, are caused by poisons generated in certain grains and generally thought to be of a chemical character. The existence of such diseases depends upon the presence of the rye or maize in which the poisons are generated;

[1] Perhaps "almost always" would be more correct than "always"; since it is at least conceivable that immune persons may carry certain disease germs, if not in their tissues, at any rate in their intestinal contents, without themselves developing the disease. Cholera and enteric fever are thought to have been spread in this way on some occasions.

ıd each of them is found in those portions of the globe only where the ›rresponding grain grows, develops the poison, and is then consumed by e people. The external influences of climate, temperature, moisture, il, altitude and the like will act in these cases mainly upon the grain, ıich may in a sense be regarded as the "external host" of the poisons these diseases. Other diseases, again, such as urinary calculus and itre, are held by some to be caused by chemical substances dissolved in inking water; and should this prove to be the case (the evidence is yet very far from conclusive), the presence and consumption of waters ıtaining these particular substances will be the most important factor the distribution of these diseases. Other disorders would seem to be ›endent upon defects or excesses of diet, or of some particular con- ıuent of the diet. To this class belong scurvy, gout, rickets, and, as ne would hold, beri-beri; and it is obvious that such diseases will y be found where the corresponding defect or excess exists. It is ıecessary, indeed, to multiply instances further; for it is after all but ruism to assert that the distribution of any disease must depend on presence or absence of its cause; though the corollary—that the dy of the distribution of any disease is a vain task unless its causation l mode of spread are constantly borne in mind—is perhaps sometimes gotten.

(B) *External or Geographical Forces.*—We have still to consider the ›ernal, or more purely geographical, forces which exert a powerful uence upon the distribution of disease. Nearness to or distance from Equator seems to be a determining factor in the distribution of some, by no means of all diseases. *The effect of latitude* is, indeed, a nplex one. It is true that the atmospheric temperature becomes ›gressively warmer from Pole to Equator, but the increase is not iform. Apart from the disturbing influence of elevation above sea- 'el, the distribution of land and sea, the effect of rainfall, winds, d other geographical conditions greatly modify the atmospheric ›nperature; and the lines of equal temperature, or isotherms, are found be by no means parallel with the Equator. Ignoring, however, for e moment these disturbing conditions, the earth may be regarded as a obe extremely cold at the Poles, and becoming steadily warmer towards e Equator. The favourable effect of warmth upon the growth of lower rms of life might warrant the expectation that all diseases caused by icroparasites would become more frequent and more severe as the quator is approached. But this is found to be the case only in a ›mparatively small group of diseases—of which malaria, dysentery, ıolera, and plague in their epidemic manifestations are the most riking examples. Many other diseases—such as whooping-cough, phus fever, cerebro-spinal meningitis, and rheumatic fever—are ore frequent, or more severe, or both, in cooler latitudes than in the opics; while at least two disorders—scarlet fever and diphtheria— e mainly met with in the cooler portions of the earth's surface, and e either altogether absent, or rare and mild in character, in tropical

and subtropical countries. On the other hand, many diseases which are absent from the higher degrees of latitude are found only in or near the tropics; these are commonly spoken of as "tropical" diseases, and form a long list. The principal examples of this group of affections are dengue, yellow fever, elephantiasis, chyluria and the other filarial disorders, liver abscess, sprue, guinea-worm disease, bilharziosis, chigo-disease, sleeping sickness, ainhum, mycetoma, tropical ulcers, oriental sore, yaws, tinea imbricata, pinta, and many other disorders, the names of which will be found in any text-book on the subject. The list of diseases that are only found in warm latitudes and are absent from the cooler zones, is a very much longer one than the list of diseases whose distribution is the reverse of this. In other words—and to sum up this paragraph—there is a greater variety and richness of disease germs in warm countries than in cold; but the disease germs which exist in both cold and warm latitudes do not of necessity become more frequent or more virulent in the warm than in the cold, and may even become both less frequent and less virulent.

This relation of disease distribution to latitude is probably to be explainedby the following considerations. The absence of many pathogenetic parasites from cooler climes may well be ascribed to the direct effect of temperature and other geographical influences, either upon these parasites themselves, in their extra-corporeal existence, or upon their extra-human hosts. Just as many tropical or subtropical plants cannot live, except under artificial conditions, in the higher latitudes, so the parasites of "tropical" diseases, or the extra-human host in which they must pass part of their lives—be it a particular mosquito, a fresh-water cyclops, a tsetse-fly, or what not—die out, unless artificially cultivated, in the cooler zones of the earth's surface. In their absence the corresponding disorder must obviously die out too. But, in the case of many of the diseases not confined to any particular zone, other factors come into play. Many microparasites of disease, while liking a certain degree of warmth, are easily killed at a temperature which is often reached by the atmosphere or the soil of the tropics. Others flourish best, both in the laboratory and under natural conditions, at a moderate degree of heat, at what is called the optimum temperature for each particular parasite; and, even if not killed at the higher temperatures, become distinctly less active. Many, perhaps all, such parasites require absence of sunlight and a certain degree of moisture to grow and multiply, and are rapidly killed by exposure to the sun's rays or by desiccation. It is easy, then, to understand that these parasites may well find the conditions of a temperate climate more suitable to their growth than those of the tropics. Moreover, if the corresponding disease is to prevail, facilities for the passage of the parasite from one person to another are essential; and the closer aggregation of people in houses in the cooler zones may be an additional factor favouring the spread of such diseases.

The same explanation no doubt holds good in regard to the *influence of season* upon disease prevalence. A large number—perhaps the majority

—of the common infective fevers are most active in the cooler season of the year, whether in cool or in warm latitudes. This is certainly the case with influenza, measles, diphtheria, small-pox, pneumonia, whooping-cough, erysipelas, cerebro-spinal fever, typhus, puerperal fever, and rheumatic affections. On the other hand, some disorders of the alimentary system, such as diarrhœa, dysentery, and cholera, are usually most active in the warmer months. Plague has generally been a warm-season disease in temperate zones, and a cool-season disease in or near the tropics. Many other affections show no very definite relations to season; probably they are obscured by the more pronounced action of other factors. In many countries the seasonal variations in the rainfall exert a more powerful influence upon disease prevalence than the variations in temperature. More particularly is this the case in India and other tropical countries, where the annual recurrence at a fixed period of "the rains" not only alters the whole course of social life, but also determines the character of the "curve" for most of the leading diseases.

The *influence of elevation above sea-level* upon disease distribution is a complex one. A high altitude implies lessened barometric pressure, lowered temperature, more direct action of the sun's rays, an atmosphere freer from organic impurities, and, in many instances, a sparse and isolated population. Each of these conditions exerts its own special influence upon the distribution of particular diseases. The lessened barometric pressure may possibly be a determining factor in the existence (it is almost certainly so in the severity) of that peculiar disease, verruga peruviana, which is only found at elevations exceeding 2500 feet above sea-level. The lowered temperature and barometric pressure together, no doubt, determine the absence of mosquitoes and other germ-bearing insects from high levels, with corresponding absence of such diseases as malaria, yellow fever, and the filarial disorders. The same factors, together with the more powerful action of direct sunlight, must exert an influence upon all disease germs; and when to these are added an isolated and scanty population, implying lessened risk of importation and diffusion of infection, and an atmosphere freer from organic impurities, it is easy to understand why such diseases as tuberculosis, cholera, dengue, and others are usually much less prevalent at high than at low levels. It must, however, be added that in some exceptional instances the disorders just named, and many others, have prevailed at very considerable altitudes. That high levels in warm latitudes may present climatic conditions—and, consequently, conditions of disease prevalence—similar to those of lower levels in cooler latitudes, is shown by the rule that typhus fever, when met with in or near the tropics, is usually seen only at comparatively high levels, whereas in the temperate zones it occurs more or less indifferently at both high and low levels.

The part played by the soil as a nidus for morbid germs outside the human body has been dealt with above; but a few words must be said as to the *influence of various kinds of soil* upon the distribution of different diseases. It would seem that what may be termed the purely geological

characters of the soil have less influence in this respect than its physical characters—such as its temperature, the amount of water contained in it, its perviousness, its configuration and exposure to sun and wind, its purity from decaying organic matter, animal or vegetable, and its relations to human dwellings. A damp, impervious soil tends to the prevalence of pulmonary tuberculosis, lung diseases of all kinds, and the rheumatic group of affections; and there is much evidence to show that this quality of the soil is the primary factor determining at least the topographical distribution of diphtheria, and, as some would hold, of cancer. A soil polluted with decaying organic matter has seemed to favour the prevalence of malaria, Mediterranean fever, yellow fever, dysentery, typhus fever, dengue, and other disorders. A marshy, undrained soil, with collections of stagnant water, provides ideal conditions for the multiplication of mosquitoes and other blood-sucking insects, and is therefore favourable to the presence of malaria, yellow fever, the filariases, and similar diseases. Cholera and enteric fever in many epidemics, though apparently not in all, have seemed to be influenced by the rise and fall of the water in the subsoil. The curve of diarrhœal disorders, particularly of the diarrhœa of infants, shows a well-marked parallelism with that of the temperature of the deeper layers of the soil. Finally, on many occasions, earth-disturbance on a large scale, as for the construction of railways or canals, has led to remarkable outbreaks of certain diseases—of which the most noteworthy have been malaria, blackwater fever, ankylostomiasis, and so-called typho-malaria.

The *influence of race* upon disease distribution is often obscured by the influence of other forces. It is frequently observed that the incidence of a particular disease is widely different upon different races living in the same place, and cannot always be ascribed to a true racial variation in susceptibility to that disease. A difference of race almost invariably implies wide divergencies in diet, housing, clothing, mode of life, exposure to the cause of the disease, acquired immunity, readiness to take precautionary measures, and the like; and each of these influences must be eliminated before the effect of true racial predisposition or the reverse can be determined. But when all these factors have been accounted for, there seems to remain, in regard to many diseases, a distinct difference in susceptibility between different races. The Jewish race, for example, is peculiarly liable to diabetes. The pure-blooded African negro is specially prone to tuberculosis, small-pox, tetanus, and epidemic cerebro-spinal meningitis. Ainhum, goundou, sleeping sickness, and the affections caused by filaria perstans, filaria loa, filaria diurna, and other parasites, are confined mainly, if not wholly, to the negro race. On the other hand, this race seems to be peculiarly insusceptible to yellow fever, and has perhaps (though the evidence on the point is contradictory) a certain degree of immunity from malaria. In the tropics generally the white races appear to be more likely to develop malaria, enteric fever, liver abscess, and scarlet fever (an extremely rare disease, in any case, in the tropics) than the coloured races; and less

likely to become the subjects of elephantiasis, chyluria, and the other filarial affections, guinea-worm disease, and many skin disorders, such as pinta, craw-craw, and tinea imbricata. The frequency of one skin disease, yaws or framboesia, seems to be largely determined by the depth of colour—or, in other words, by the amount of pigment in the skin—of different races. The Mongolian race is remarkably susceptible to many of the acute and chronic infective disorders; and a few animal parasites, such as the distomum pulmonale and distomum sinense, are apparently confined to this race.

The *movements of mankind* are among the most powerful influences in the distribution of disease. On innumerable occasions emigrants, traders, and explorers have brought small-pox, influenza, measles, syphilis, and many other diseases to countries, islands, or isolated communities where they were before unknown. Emigrants have carried relapsing fever, leprosy, and hydatids from the Old World to the New. Imported labourers from China have been the principal means of diffusing leprosy in Australia, the Malay Peninsula, and the Far East generally. The annual movements of Russian peasants, who leave their villages to obtain work in other—often distant—parts of the country, have frequently aided in the spread of cholera, syphilis, ophthalmia, and other maladies. Plague, beri-beri, epidemic cerebro-spinal meningitis, and many other diseases have been repeatedly carried by sea or land over vast distances, and even from one hemisphere to another.

There have been few more potent agencies in the diffusion of disease than pilgrimages to various religious centres. At the present day, the most important of these pilgrimages are the great bathing festivals at Hardwar, Benares, and elsewhere in India—festivals which have been known to lead to a gathering of two or three million persons; the incessant flow of pilgrims and corpses to the Shiah holy burying-grounds of Kerbela and Nedjef, in Mesopotamia; the Moslem pilgrimages to Meshed and other shrines in Persia, Mongolia, and elsewhere; and the annual Moslem Haj, or pilgrimage to Mecca and Medina. Cholera, plague, small-pox, and other diseases have been repeatedly spread by these means; and it has been one of the principal aims of successive International Sanitary Conferences to devise measures to lessen this danger.

The movements of men in time of war—though here combined with conditions other than mere movement—have greatly contributed to the prevalence and spread of many diseases. Enteric fever has been the scourge of almost all armies; small-pox, typhus fever, malaria, so-called typho-malaria, measles, scurvy, and other diseases have on countless occasions attacked armies in the field or the population of beleaguered cities. Typhus fever is said to have been widely diffused in Europe during the Napoleonic wars, and to have diminished greatly when these came to an end in 1815. The same disease was seriously epidemic among the refugees in Constantinople during the Russo-Turkish campaign in 1878. Leprosy was spread in the Near East as a result of the disturbances in Crete in the latter years of the last century. The Crusades—half-

pilgrimages, half-military expeditions—are thought to have aided in diffusing many diseases; and, indeed, there has been no war in ancient or modern times from which examples analogous to these might not be cited.

Among the forces at work in determining disease prevalence, a prominent position must be given to the conscious *efforts of mankind to control or extinguish disease.* It is no longer open to question that many maladies can be prevented by properly devised measures; and that, other conditions being equal, these maladies will be less or more prevalent in proportion as those measures are or are not enforced. Public health measures—whether of a general character, such as cleanliness, drainage, the provision of water supplies, building laws, and the like, or of a special character, varying with each particular disease—must, therefore, be regarded as factors of real importance in the distribution of the "controllable" diseases. In regard to many, indeed, they are, or may be made the primary factor, yielding place to no other. The experience of many years in England — where more extensive and costly efforts have been made to improve sanitation and control disease than in any other country — has shown that a high level of public health administration, the strict application of a good sanitary law, and the execution of great general sanitary measures in town and country, can practically extinguish dysentery, malaria, and typhus fever. They have led to a marked diminution in enteric fever and pulmonary consumption; and they have kept at bay cholera and plague—diseases which though repeatedly brought to her shores, have not in recent years gained a footing in the country.

The effect of special measures to control particular diseases has been no less marked. The drainage and cultivation of marshy lands has practically exterminated malaria in Holland and England; and similar measures, combined with a systematic attack on the malaria-bearing mosquito, have led to the same result in many places in Italy, in Cuba, on the West Coast of Africa, at Ismailia on the Suez Canal, and elsewhere. Yellow fever has been all but extinguished at Havana, solely as the result of efforts to check its spread by mosquitoes. Cholera, dysentery, and enteric fever have been repeatedly controlled, and even made to disappear altogether, by the provision of a good water supply and the prevention of contamination of drinking-water. Surgical erysipelas and hospital gangrene are almost unknown, since the introduction of improvements in hospital building and management, and of antisepsis and asepsis in the treatment of wounds. Trichinosis has been stamped out in many countries by systematic meat-inspection. The muzzling order and other measures have led to the almost complete disappearance of hydrophobia in England. Small-pox ceases to exist where efficient vaccination and revaccination are enforced; and the recently introduced methods of preventive inoculation against enteric fever and plague seem undoubtedly to affect the local incidence of these diseases, and are thus important factors in their topographical, if not

in their geographical distribution. Scurvy, relapsing fever, and typhus fever are amenable to control by attention to diet, cleanliness, proper clothing and housing, and the prevention of overcrowding. On the other hand, in places where no attempt is made to repress special diseases, and where general sanitation and public health administration are unknown, or at a low level, every one of the diseases just named, and a host of others, may and do prevail to an almost unlimited extent.

The use of maps in medical geography.—In conclusion, a word must be said on the value of maps in illustrating the geography of disease. "Spot-maps," or shaded or coloured plans of a village, a town, or even a comparatively large district, are constantly employed to show the topographical distribution of a disease in a given epidemic, or during a certain definite period. For this purpose they are invaluable, and will often bring out, more rapidly and clearly than any written description could do, the relation of the disease to local conditions—such as elevation, configuration or geological character of the soil, a particular water supply, or social or racial divisions of the population. But the attempt to construct maps of disease prevalence for still larger areas—as for whole countries or continents, and, *a fortiori*, for the whole world—presents certain difficulties and pitfalls which are not always easy to avoid; and such maps may even tend to mislead rather than to instruct the student. There is, *first*, the truth, to which attention was called above, that no disease has a permanent distribution, unless it be ubiquitous, in which case a map is superfluous. Disease maps should, therefore, always bear some indication that they refer to a particular epidemic or to a particular limited period of time. There is, *secondly*, the difficulty that, unless on a gigantic scale, world-maps must necessarily show only in the most general way the physical and other variations of the surface of the globe. The conclusions such maps may seem to justify, on the relation of any disease to these variations, will often be of great value; but these conclusions should always be controlled, and will very often be modified, by a consideration of the behaviour of the disease over smaller areas. In other words, the study of the "geography" of a disease and the study of its "topography" should always go hand in hand. There is, *thirdly*, the difficulty that, in regard to almost every disease, information as to its presence or absence is invariably lacking from some—often large—portions of the earth's surface. These portions should not be left blank, since that would indicate definitely the absence of the disease; they should show, either in words, or by some conventional sign, that information is lacking. There is, *fourthly*, the difficulty that, if a disease map is to be of any real use, it should show, by shading or colour or other sign, the *relative incidence* of the disease in different areas. Yet, as already shown, the means for obtaining accurate knowledge of the relative frequency of any disease is more often than not wholly lacking. This is certainly the case with vast areas of the earth's surface, whence no statistics of scientific value are forthcoming. Even the definite statement that a disease is "absent" may sometimes (as in the case of ankylostomiasis)

only mean that it has not been looked for with the means of precision now at the disposal of science; while the significance of such terms as "rare," "frequent," or "common," when applied to disease prevalence, must vary widely in different countries and with different observers. It is clear, therefore, that a perfect world-map of any disease is at present unattainable. Even if maps are carefully constructed, and accurately reflect our knowledge or lack of knowledge of a particular disease, their value is but relative. They should, I venture to assert, never be studied alone, and without a good verbal description of the distribution of the disease in relation to its etiology and mode of spread.

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NURSING

By Miss Amy Hughes

Tending the sick has risen to the dignity of a profession, and special training is required for those who undertake it. The keynote of good nursing is intelligent obedience, only obtainable by systematic education. Women who wish to be nurses need practical skill, powers of observation, sympathy, and tact in dealing with various idiosyncrasies. They must also remember that time is needed in which to gain these qualities and the knowledge which experience alone can give.

Hospitals and infirmaries, which offer facilities for regular instruction, have become training schools for nurses. Order, method, punctuality, obedience, are part of the groundwork of a training school; but to these must be added thoroughness, promptness, accuracy in observing and

correctness in reporting observations, and a loyal attitude towards doctors and patients. The whole system of trained nursing depends upon the maintenance of this attitude. Nurses are bound, by their position, to render loyal obedience to medical men. It is not their duty to suggest or initiate treatment of any kind, except by express permission or in some sudden emergency. They have no responsibility save that of faithfully obeying orders, and the higher the discipline the more readily this is recognised.

General Hospital Training may be divided into surgical and medical work. The probationers are moved from ward to ward at the discretion of those in charge; for the sake of order and discipline, this power should be vested in the matron, herself a trained nurse, who is guided by the reports of the "sisters" or "charge nurses" of the different wards.

The demands upon physical powers and mental assimilation are alike heavy, and should not be undertaken too early in life. From twenty-three to twenty-four is the earliest age at which a nurse should begin her training, even in children's hospitals. The actual strain of lifting, moving, etc., may not be so heavy; but the incessant watchfulness, cheerfulness, and absolute self-control necessary in dealing with children are a heavier task than is usually supposed.

Surgical Ward Work.—*Ventilation.*—The first essential in a surgical ward is pure air, the second absolute cleanliness. On the nurse devolves the management of windows and ventilators so as to obtain the maximum change of air with the minimum of draught. Common sense must be brought to bear on the matter; the direction of the wind and its effect on the ventilating arrangements of the ward must be considered, so as to avoid a through draught, also the nature of the warming apparatus, whether open fireplaces or hot pipes, and its position with regard to doors and windows. The usual temperature—from 55° to 60° F.—should be recorded at regular intervals during the twenty-four hours, and freshness must be equally maintained day and night. *Absolute cleanliness* applies to every detail of a ward, from the patients and their beds to the smallest appliance and fitting. Dusting means not merely moving the offending material, but removing it from every part of the walls, floor, furniture. A damp, not wet, duster is most effectual; and, if desired, it can be moistened with a disinfectant. Floors should be sprinkled before sweeping, and the bedstead of every patient dusted daily. Every appliance must be scrupulously cleansed, no stains nor fur allowed on utensils, test-tubes, etc.; strong soda water or spirits of salt (applied with a mop) will clean any glass and earthenware vessel, but the latter must not be used for metals, nor for lavatories on account of the metal fittings. Bedsteads, bedding, mackintoshes, splints, etc., must be kept absolutely clean.

Surgical cleanliness has a higher ideal than general cleanliness. It aims at the destruction of bacteria, and, if possible, at their complete absence (asepsis). This is attained by boiling all glass and metal

appliances for twenty minutes, maintaining the temperature at 212° F. Dressings, sponges, wool-pads, are sterilised by means of steam in a special apparatus, and kept hermetically sealed until they are needed ; antiseptic dressings, such as medicated gauzes, must be equally carefully guarded from exposure to the air, if not sterilised again before use. The most careful watchfulness is demanded from the nurse, that she does not nullify these precautions by any careless action, such as laying down a dressing, scissors, or any appliance on an undisinfected surface. She must herself be scrupulously clean in person and dress, and her hands must be carefully kept, with short clean nails.

Cleansing of Hands.—In attending upon the surgeon, or in preparing for dressing cases, the hands should be first thoroughly washed in hot water, using a sterilised nail-brush and soap freely. The hands and fore-arms are then soaked for a couple of minutes in an approved antiseptic lotion, and may then be considered as cleansed. Contact with anything that is not sterilised will render this treatment useless, and the whole process must be gone over again.

It is important that nurses should have a knowledge of the various *strengths of disinfectant and antiseptic lotions*, and should understand their preparation from concentrated solutions and tablets.

(a) *Perchloride of mercury* is used 1 in 1000 for hands, from 1 in 4000 to 1 in 8000 for douches, wounds, etc. ; other strengths being specially ordered. Metal instruments should be wiped at once if immersed in it, or they will turn black.

(b) *Biniodide of mercury* is used in the same way, and of the same strength. A 1 in 500 solution in spirit is used for disinfecting hands before an operation.

(c) *Carbolic acid* lotion is used 1 in 20 for hands, instruments, and external washing of sound skin ; 1 in 40 and 1 in 60 for wounds, etc.

(d) *Condy's fluid*, ʒj to Oj (or three to four crystals of permanganate of potash to 1 pint) for douches, wounds, etc. ; it stains linen, instruments, and hands.

(e) *Saturated solution of boracic acid*, about 4 per cent, for wounds.

(f) *Sanitas*, ʒj to Oj, a pleasant deodorant for foul wounds, and for cancer, gangrene, etc.

(g) *Creolin*, ʒj to Oj for hands and instruments ; must be mixed with a little cold water before adding hot, and can be used with soap. Same strength useful for irrigating wounds.

(h) *Izal* and *lysol* have similar properties, and are used as disinfectant lotions, 1-100.

Poison Bottles and Lotions.—Every poisonous lotion should be in a special bottle with conspicuous label, and kept under lock and key ; any possibility of confusion with medicines or beverages, whether in or out of use, should be prevented. The bottles should be specially ribbed, so that they can be recognised in the dark. Corrosive sublimate is usually coloured pink or blue to avoid mistakes ; the other lotions, except boracic lotion, have each a distinctive and easily perceptible smell.

If a nurse has *dressings* to prepare for granulating wounds, the lint or gauze must be cut exactly to cover the sore, to avoid softening the edges. Ointments must be very thinly spread, and never be allowed to accumulate on the sound skin. If a moist dressing is ordered, a piece of gutta-percha tissue considerably larger than the lint must be applied over the lint, no portion of which should be left uncovered; but if an evaporating lotion be required, the tissue must be omitted, and the application frequently changed and never allowed to dry. In washing or syringing a wound, a receiver must always be placed to collect the water or lotion that has touched the sore; and if wool is used to cleanse, each piece as used must be placed in a receiver, and never dipped again into the lotion. To place the foot of an ulcerated leg, for example, in a basin of disinfectant and to use one piece of wool to cleanse the wound and surrounding skin is not surgical nursing.

In dressing burns the fresh application should be ready to put on as the soiled one is removed; thus unnecessary exposure to the air, which causes great smarting, is avoided. In all dressings the nurse must observe strict cleanliness in every detail. Soiled dressings should always be removed by forceps, placed in a receiver at once, disposed of in the manner of the hospital, or burned without delay. The forceps must be cleansed with a nail-brush in soap and water, boiled, and dipped into a disinfectant before being used again. Windows should always be closed when a dressing is being done, and every wound should be covered as quickly as possible.

In offensive cases, inhalation of the odour must be avoided, and the patient should never be made to feel the unpleasantness, of which he is, as a rule, only too fully aware.

Cancer patients vary greatly, and by observing that which suits each special case much pain may be avoided. In dressing extensive cancerous surfaces a styptic should be at hand in case of hæmorrhage; in these cases, and for gangrene, burns, and similar conditions, gentle, firm handling is needed, combined with quickness and lightness in removing and reapplying dressings.

In *padding splints*, evenness is ensured by lacing the padding down the back of the splint with strong thread, so that it can be regularly tightened. Special care must be given to ensure the edges being well protected, or pressure sores may arise. Children's splints, and others likely to be soiled, can be covered in addition with jaconet, which is easily cleaned. In *preparing for extensions* the nurse must have ready a long, even strip of strapping (preferably on holland), known as the stirrup, cut with regard to the width and length of the limb; also two or three thin strips long enough to go at least twice round the limb diagonally, to avoid any arrest of circulation: the block, pulley, cord, the weight ordered, sand-bags, and a couple of thin flannel bandages must also be at hand. When an extension is to be applied in cases of hip disease, the ends of the stirrup must be well above the knee (quite half-way up the thigh), and the loop so arranged that its sides are exactly equal in length,

the block and cord with the attached weight being in the centre. The block is easily fastened to the stirrup by a length of strapping extending from above the ankle on each side, and is applied with its adhesive side to the stirrup, so that the block is enclosed between the strips. It may be further secured by a strip wrapped round on each side of the hole through which the cord passes. The strips which keep the stirrup in position must not be too tight, and the edge of the lowest one must be kept from chafing the skin just above the heel. The patient must be kept flat, with only one pillow, the foot of the bed raised, and the limb retained in position by sand-bags; careful washing and powdering are necessary, when the extension is changed, to prevent chafing of the skin, turpentine being used to remove the adhesive material from the skin.

Bandages.—The nurse must be able to make the various bandages required. Those most commonly used are the roller, the T, the triangular, and the many-tailed bandages. The art of bandaging, acquired intelligently after due anatomical instruction, is very important. The bandage should be gently but firmly applied, alternate slackening and tightening avoided, also any jerking or pulling. In dealing with an injured limb, it should be lightly yet firmly grasped, supported as much as possible, and moved evenly. To carry it on the palm of the hand gives less pain than holding it in the fingers.

In **Receiving Accident Cases** in a ward, orders will be given as to bathing, etc. If the accident be a fracture, fracture boards must be placed under the mattress in the bed, and the splints suitable for the case, according to the use of the hospital, should be ready, and, if necessary (that is, in fractures of thigh), an extension prepared. In removing the clothes the patient must be kept recumbent, to avoid syncope from shock, and the garments removed as gently as possible. Trousers, coat-sleeves, shirts, socks, can all be divided at the seams, and lifted from the injured parts, which should always be freed first. The same applies to a woman's garments; skirts can be slipped downwards by raising the back slightly, and by pushing down the bed underneath to make room for them to be drawn away.

The necessary washing must be done between blankets, one being placed on the bed before the patient is laid in it, and another over him; the nurse must be on the watch for signs of exhaustion. Turpentine is useful to remove stains from the hard skin of hands, feet, and knees, but it must be well washed off with soap and water to avoid irritation. Except in the neighbourhood of scalp wounds, hair must never be cut without a direct order from the doctor. In head injuries the nurse must report any discharge from ears or nose, any peculiarity of the eyes; and if there are fits, she must specially observe where the convulsive movements start. In abdominal cases, swelling, tenderness in any special area, bruises, cuts, scars, wounds, ulcers, skin eruptions, vomiting, discharges, or hæmorrhage, in fact, anything at all abnormal, must be reported. After washing, the blankets are removed, and if the patient

be cold or collapsed, hot bottles securely covered in flannel may be applied to the extremities. Fractured limbs must be steadied by sand-bags, and if the bed-clothes press on any injured part, a cradle must be used to support them. Stimulant must not be given without direct orders.

In **Preparing a Patient for Operation,** the nurse acts under the orders of the surgeon; it is usual to give an aperient over-night, a simple enema early in the morning, and no solid food or milk for at least four hours beforehand, a cup of good beef-tea being given about two hours before the appointed time. If a woman, the hair should be arranged in two plaits for future convenience, and the catheter may be ordered shortly before the operation. Ordinary bed-clothes are usually worn, with a special wrapper. All false teeth must be removed. The preparation of the skin, not merely at the seat of operation, but for a considerable distance round, is carried out according to the orders of the surgeon, but the routine is usually much the same. The skin, if hairy, is shaved, and then thoroughly cleansed with a sterilised nail-brush, soap, and hot water, to which is frequently added a little washing soda. It is then rubbed with turpentine or ether, to remove all greasy secretions, and finally is covered by a dressing soaked in a suitable disinfectant lotion, covered with protective: 1 in 2000 perchloride of mercury lotion is frequently used, and the dressing left on from six to twelve hours.

The arrangements at the operation depend on the custom of the hospital; but the nurse is often required to wash sponges, hand instruments, and even to support a limb. A low pillow is usual, with small mackintoshes and towels which have been previously sterilised. The temperature of the theatre averages from 65° to 70°, and is even higher in cases of severe abdominal operations; but this is a matter entirely to be decided by the surgeon. Avoidance of draughts is essential. Sterilised sponges which have been subjected to a special process, or pads of absorbent gauze and cotton wool, previously sterilised, are usually employed. If placed in an antiseptic solution, they should be squeezed as dry as possible before being handed to the surgeon, and the exact number should be carefully counted. It is absolutely necessary to be certain that the number of the sponges at the end of the operation is the same as at the beginning. Stimulants should be at hand at every operation, together with a hypodermic syringe; also the materials necessary for the infusion of saline solution.

After-care of Operation Cases.—The bed to which the patient is taken must be well warmed by hot bottles, which must be properly enclosed in flannel bags to prevent the risk of burns while the patient is unconscious, and a warm water-pillow may be ordered. A receiver and a couple of soft towels must be in readiness in case of vomiting after the anæsthetic.

In moving a patient back to bed, the head should be kept as low as possible, and careful attention given that before complete consciousness is recovered the dressings are not disturbed. The patient should not be

allowed to raise himself hurriedly, for fear of hæmorrhage or syncope. In amputation cases a tourniquet should be within reach of the nurse, to be applied if hæmorrhage occurs, until the surgeon can be summoned. Every detail regarding nourishment, stimulants, opiates, use of the catheter, and so forth, must be obtained from the surgeon. The pulse should be felt immediately after the operation, in order that it may be reported ; and note must be taken of the colour of the face and lips, and the character of the respirations.

The dressings should be inspected at frequent intervals, and if discharge or blood soak through, the fact should be reported at once. If the surgeon be not at hand, the dressing should be "packed"; that is, pads of sterilised absorbent wool should be bandaged over the points where the discharge appears.

Ice to suck, or hot water in quantities varying from a teaspoonful to half a pint, is usually ordered to relieve excessive thirst. After severe hæmorrhage the thirst is sometimes allayed by a rectal injection of warm water.

The nurse should have all in readiness for the *visit of the surgeons to a ward.* Hot water, towels, disinfectant lotion for hands and instruments, dressing forceps, probe and director, and a tongue spatula immersed in lotion should be carried round by the nurse ; and artery forceps, bistoury, etc., should be in readiness if required : a good lamp should always be ready ; and a receiver for soiled dressings, the clinical notes beside each patient, splints, etc., so that no unnecessary delay is caused.

Medical Nursing.—The ventilation of medical wards is most important, as the temperature is usually from 60° to 65°, or even 70° F.—and yet the air must be kept quite fresh. It is advisable to have two or more thermometers in each large ward, to ensure an evenly distributed heat. In small wards, if a moist and high temperature is required, draughts may be avoided by the Hinckes-Bird method of ventilation. A piece of wood, three or four inches deep, exactly fitting the window-frame, is placed so that the lower sash closes on it, and the outside air passes up between the upper and lower sashes in the middle of the window, and is directed upwards into the room.

The use of the *clinical thermometer* needs greater care to ensure accuracy than is often bestowed upon it. If given to a patient able to hold it in the mouth, it must go under the tongue and be held by the closed lips (not by the teeth), always for the same time—usually five minutes. If placed in the axilla, the skin must first be dried, and the thermometer so inserted that the bulb touches the skin on every side, the arm being drawn across the chest. If necessary, the arm must be held there for the required time. In children the fold of the groin is often convenient, or the rectum. In every case the record should be written down at once in a book kept for the purpose, and the thermometer dipped in a cold disinfectant solution, and then in cold sterilised water, before being given to another patient. The temperature of a patient in a bath or pack must not be taken in the groin or axilla.

Accurately counting the rate of the *pulse* and reporting its character are matters of training and experience, and of great importance. A nurse should be able to recognise the more important changes; also whether drugs, stimulants, baths, produce any marked effects.

It is better not to let the patient know when the *respirations* are being counted, as this may alter the rate. The nurse must be able to note and report any changes that may occur; attacks of dyspnœa, sighing respirations, stertorous breathing, and Cheyne-Stokes breathing are all important indications in various diseases.

Bed-making is one of the important duties of a nurse. In hospital wards, where the beds and mattresses are of right size and height, no special difficulties arise. A single blanket is spread over the hair mattress, and over this a sheet, the upper end of which is rolled round the bolster, not spread over it, and tucked firmly in all round. A draw-sheet, consisting of a sheet folded about three feet wide, is placed across the bed, one end being tucked in at one side, and the extra length flatly folded and tucked in on the other. If necessary, a square of mackintosh is placed under the draw-sheet, and may conveniently be kept in place by a small safety-pin at each corner. The top sheet and each blanket should be put on and tucked in separately, and the feelings of the individual patient consulted as to folding back blankets or quilt at the top. The quilt should be so pinned or folded that it does not touch the floor at the bottom or sides of the bed, and prevent free circulation of air underneath.

In *changing bed-linen* for a helpless case, the upper sheet and quilt must first be removed, and the patient covered by a blanket; he must then be gently turned on one side (if possible the right, to avoid any risk of syncope in cardiac or pleuritic affections). This can be done with little effort by means of the draw-sheet; this is then, with the mackintosh, rolled up tightly towards the patient, the bottom sheet untucked, also rolled up tightly, and with the other pushed well under the shoulder and buttocks of the patient. The clean sheet, draw-sheet, and mackintosh are also rolled up together lengthwise for half their width and placed close to the patient, the other portion being smoothly spread over the bed. For a weak patient this is a good opportunity for washing the back and applying spirit and dusting powder, so that he need not be disturbed again. The patient is then turned back over the rolled linen, and just turned sufficiently on the left side to allow the soiled linen to be removed; the clean roll is then drawn through and evenly spread over the other half of the bed, and all well tucked in. It facilitates matters to raise the feet and legs, and place them on the clean linen before turning the patient back; and the head should always be comfortably supported by pillows. The top sheet can be passed in under the blankets from the bottom of the bed, and then they are separately tucked in and the quilt replaced. By placing the rolled part of the sheet next the bed the hands can be slipped underneath it, palms upwards, to draw it through; thus the nurse's knuckles are not pushed against the back of

the patient. Heavy bed-clothes must always be avoided, and the feelings of the patient consulted as to warmth whenever possible.

In *removing body linen* of helpless patients, it is well to draw it up from the back, and, having unfastened the collar, to bring the garment over the head, taking the arms out of the sleeves last. Putting on fresh linen is easier if the arms be first placed in the sleeves, and the garment then lifted over the head, and drawn down at the back. Where all movement is undesirable, a shirt or night-dress can be divided down all the seams of one side—neck, shoulder, sleeve, etc.—and fastened by tapes; it has then only to be put on at one side, and the back rolled and passed under the patient like a draw-sheet.

Medical Examination.—The nurse must be ready to remove and adjust all personal or bed clothing for medical examination. When the abdomen is to be examined, the quilt and blankets must be turned back, but the sheet left upon the patient for the medical man to arrange for his own convenience.

Helpless Cases.—In changing the bed-linen of cases which must not be turned at all on either side, the dirty under-sheet, with mackintosh and draw-sheet, can be rolled up from the bottom of the bed, and pushed well under the buttocks; the rolled part of the clean linen is now laid close to it, and the lower part of it spread and tucked in at the foot of the bed. By gently raising the buttocks the two rolls are passed underneath, and the patient now rests on the clean sheet. The upper part of the soiled sheet is then rolled and pushed well up under the shoulder-blades, and the clean one also; and then, by gently raising the shoulders a very little, both are drawn up to the top of the bed, the dirty linen removed, and the clean spread smoothly. By changing from below upwards, the patient is not pulled down in the bed, which would entail the extra fatigue of being lifted up again.

Lifting is readily done by two persons, who pass hands—left or right, as the case may be—under the buttocks, and the other hands just below the shoulder-blades; while a third helper, if the patient be very weak, supports the head and shoulders. By lifting *exactly simultaneously* the heaviest patient can be raised without over-exertion. Or two assistants may grasp the draw-sheet close to the buttocks and under the shoulders, the head being supported as before, and the patient raised; but this is apt to bring the draw-sheet too far up the bed, and the patient is pulled down again in endeavouring to rearrange it. A pillow is useful in abdominal cases where the knees are drawn up; and it can be efficiently protected by placing a piece of mackintosh round it under the pillow-case. When the patient is inclined to slip down in the bed, a bolster, similarly protected, may be substituted, a strip of bandage being attached to each end and tied to the bed-head. When a pillow is used to support a limb, it is more comfortable if hollowed in the middle so as to form a trench.

When a *cradle* is used to keep off the weight of the clothes, a thin blanket or the sheet should be next the patient.

Water-beds and water-pillows are filled with water at a temperature of

90° F., so as neither to chill or overheat the patient. Care must be taken that while not too full, they are yet full enough to prevent the patient's weight displacing the water, or he will practically rest upon the mattress beneath. They should be covered by a mackintosh and thin blanket under the sheet. A water-bed must be filled before the patient is placed on it, but a water-pillow can, if necessary, be slipped in empty, and filled with the patient lying on it. Care should be taken that the patient is in the middle of a water-pillow, for if allowed to rest on the edge bed-sores will form. Air-beds and air-cushions are also useful.

Bed-rests are helpful when it is necessary for the patient to be more or less upright. Special care is needed in such cases to prevent the formation of bed-sores, as extra pressure is thrown upon the sacrum and buttocks, and the circulation of such patients is usually defective.

When a patient has been ordered to be placed between blankets, as in acute rheumatism, those next him should be frequently changed, and a draw-sheet be always used to keep the back in a good state. Flannel night-shirts must be worn.

Bed-sores.—The prevention of bed-sores consists in cleanliness, dryness of the skin, smoothness of the bed-linen, and in avoiding undue pressure on any part. Except, perhaps, in some rare cases of spinal disease, when they are said to form with appalling rapidity, bed-sores are *always* preventable; indeed, it is with some hesitation that I allude to any possible exceptions.

Constant cleanliness and watchfulness, a vigilant eye for discharges, attention to the smoothness and dryness of the sheets, and judicious changes of position are the essentials for their prevention. The use of water pillows or beds is imperative in long or severe cases, and, being made of smoother material, are preferable to air beds or pillows; they are also more elastic. All parts exposed to pressure must, at least twice daily, be washed with soap and water, well dried, thoroughly rubbed with spirit, and dusted with powder. A useful mixture is one part boracic to two of starch powder. If inclined to be tender, the skin may be painted with collodion or balsam of Peru. When it is difficult to maintain dryness, lanoline or zinc ointment may be rubbed in and powdered. In all cases the rubbing should be very thorough, so as to improve the circulation of the parts, and when ointment is employed to ensure its absorption by the skin. Ring-cushions may be made to relieve the pressure on heels and ankles, if a water-bed is not used.

Dryness of Bed.—When there is no control over bladder and rectum, careful and frequent cleansing and changing are necessary. Incontinence of urine may be met by the use of glass urinals for both male and female cases, supported by pads of wood wool or carbolised tow in butter muslin; in the former cases care must be taken to avoid pressure on the scrotum, and in both absolute cleanliness and frequent dusting with powder are essential to avoid chafing. In female cases the vulva, particularly within the labia, must be carefully attended to. When there is loss of control over the rectal sphincter, similar pads on a piece of mackintosh may be

advantageously used; they can easily be removed, destroyed, and new ones applied. In some cases where there is a danger of hæmorrhage these absorbent pads are ordered, in order to avoid the movement entailed by placing the patient on a bed-pan. In washing stout patients, especially women, the parts under the breasts and the folds of the groin and thighs need careful drying and powdering, as neglect may soon cause eczema or painful sores. Nurses cannot have too constantly before them the suddenness with which sores may appear after what may seem to them but trifling neglect.

When bed-sores have formed, the treatment is in the doctor's hands. For merely an abrasion of the skin a simple dressing is ordered, protected by lint or a pad of gauze, and secured by strapping. The bony prominences may require protection by pads made of several layers of lint, with a hole in the centre over the wound, secured by strapping, and not removed, if possible, for two or three days. If a slough has formed, the nurse may be ordered to apply antiseptic fomentations, which are cut so as to exactly cover the sore. After the slough has separated, the cavity may be dressed with antiseptic gauze, or dressings of resin, zinc, or other ointments; in such cases the dressings must be laid on the wound only, special care being taken not to soften the surrounding skin.

The doctor requires faithful **Reports** of all that occurs to the patient between his visits—hence the importance of a nurse trained to accurate observations and statements, familiar with symptoms, and aware of their practical indications.

For example, in enteric fever a report should deal with the following points:—(1) Temperature, every four hours, in mouth or axilla, as desired. (2) Pulse, at same intervals, with statements as to strength and variation, if any, at stated times, or after food, drugs, stimulants, etc. (3) Respirations, at same intervals; cough is important as a warning of lung complications. (4) Stools. Frequency, colour, and character, noting if undigested food be passed, blood, etc., and if much flatulence. (5) Amount of urine, and its colour—any symptoms of retention. (6) Vomiting; frequency and nature. (7) Any eruption, abdominal pain, tenderness, or distension. (8) Exact amount of sleep; its character—restless or quiet; whether delirium, muttering, twitching of muscles; also manner of waking—quietly, or with a start. (9) Condition of skin, dry or moist—of tongue, amount of sordes on teeth. The mouth and teeth should be frequently cleansed by lint or linen, wrapped round a piece of wood or forceps, dipped in the prescribed lotion, and gently passed round the mouth. If able, the patient should also be encouraged to rinse the mouth and gargle. (10) The exact kind and amount in ounces of nourishment taken, the hours when it was given, and the patient's inclination for it; the amount of stimulant and medicine, and the times of each. (11) Effect of any drug prescribed for temperature and pulse; if for sleep, when sleep was induced, how long after, and for what length of time. (12) Effect of sponging; when done, for how long, and the result on the temperature, pulse, respiration, sleep, and general condition.

Such a report should be written both by the day and by the night nurses, and read by both, to ensure that no important change is overlooked.

Effect of certain Drugs.—The nurse should be able to recognise the more important effects of these :—

Opium and morphine—drowsiness, contraction of the pupils, bad breathing, and constipation.

Arsenic may produce vomiting, diarrhœa, and, when taken for a considerable time, weakness, paralysis of the limbs.

Quinine—headache, deafness, noises in the ears, and occasionally a rash.

Salicin or the salicylates—deafness, headache, excessive perspiration, and vomiting.

Mercury—tenderness of the gums, salivation, and diarrhœa.

Belladonna and atropine—dry throat, dilatation of the pupils, and sometimes a rash and delirium.

Antipyrin and antifebrin—symptoms of collapse.

Bromide of potassium—occasionally a rash.

Iodide of potassium may produce the symptoms of a severe cold, with running at the eyes and nose, and sometimes a rash.

Carbolic acid—greenish urine.

Turpentine—blood in the urine and pain in the back.

Examination of the Urine.—The nurse should be able to report intelligently on the colour, deposit, and reaction of urine.

Administering of Medicines.—In administering medicine, the nurse should ascertain whether it is to be given before or after food. Certain drugs are given at certain times. Quinine and alkaline mixtures are usually taken before food ; cod-liver oil, iron, and arsenic after.

All medicines must be accurately measured in a graduated glass, as spoons vary greatly in size. The bottle should be shaken, and the contents poured out away from the label. "Drops" must always be measured in a minim glass. The glasses must be washed directly after use, and, in a ward, between each patient. Medicine bottles should *never* be put down near lotion or liniment bottles.

Special Applications.—The numerous special applications required in nursing should be thoroughly familiar to a trained nurse.

Poultices.—In making a jacket poultice the nurse must prepare two pieces of calico, shaped at the neck and under the arms, so that the poultice covers the sides of the chest from the armpit downwards. Two pieces of thin mackintosh, a little larger and similarly shaped, sufficient cotton wool to cover both chest and back, a poultice jacket, safety-pins, linseed meal, a spatula (ordinary painter's), a basin, and boiling water are also needed, and, if the poultice be made at any distance from the patient, two hot plates. The basin and spatula must be heated, sufficient boiling water poured in to make the required poultice (about ¾ pint for an adult), and the linseed sprinkled in, being well stirred all the time. A well-made poultice when turned out should leave the basin quite clean. The mixture is then quickly and evenly spread by the spatula, the edges

of the calico (not more than half an inch wide) being neatly turned over, the poultice rolled up, placed between the hot plates if necessary, and brought to the patient. He must previously have been placed on one side, with the night-shirt ready to be pulled well up at the back, if he be too weak to have it removed. The poultice is then half unrolled, and applied, care being taken not to injure the skin, though this is not likely if it is not too wet. It is next covered with the jaconet and a layer of cotton wool (both half rolled), also with the poultice jacket; the shirt is then pulled down, the patient turned on his back, and the rolled part of poultice, wool, etc., brought round to the other side. The front half of the poultice is made in the same way, applied to the chest, covered with jaconet, wool, and the jacket; then both are secured by safety-pins on each shoulder and down the sides, the poultice jacket being pinned down the front. The shirt is drawn down, and the patient should have some nourishment after the fatigue. Well-made poultices thus applied retain their heat for many hours. A little oil spread over the linseed is soothing if the skin is becoming tender.

"*Poultice*" or "*pneumonia jackets*" are garments made of a strip of thin flannel or flannelette, the right width for the patient, shaped at the neck, and well cut out under the arms, meeting in front and overlapping a little. They are lined with a layer of cotton wool neatly tacked in, and can easily be placed over the poultice, secured on the shoulders and down the front by safety-pins, which are firmer and more comfortable than tapes. In bronchitis cases this is useful, and the poultices can be changed without removing the jacket. In pleurisy a band of flannel pinned firmly round the lower ribs gives relief by restraining muscular movements.

Mustard poultices are conveniently made by adding the proportion of mustard to the boiling water, and then stirring in the linseed. Mustard plasters are made by spreading thickly mixed mustard on a square of brown paper of the exact size ordered, and covering it with a piece of muslin. Mustard and the proportion of flour ordered may also be mixed and applied in the same way. Mustard leaves are dipped in tepid water and placed on the spot. These applications are left from ten to twenty minutes, as ordered; and, after removal, the skin must be covered with a layer of cotton wool.

Bread poultices are conveniently made by placing the crumb of white bread (stale if possible) on a piece of calico or small towel across a basin, pouring boiling water over it, wringing as dry as possible, placing between muslin, and applying, with jaconet and wool over, as before.

Blisters.—Before applying blistering fluid the skin should be well washed with soap and water, and, if necessary, with ether, to remove the natural greasiness, and the outline of the area painted with vaseline or oil to prevent the fluid running beyond the indicated area. The cover of cotton wool must not be strapped at all tightly, or pain will ensue as the blister rises. If either a plaster or blistering fluid be used and a blister does not rise within a reasonable time, a poultice or fomentation

may be applied, and usually has the desired effect. If ordered, a snip is made at the lowest part of the raised cuticle, and wool arranged to catch the fluid; if desired for examination, this must be caught in a test-tube. If the blister is to be kept open, the raised skin must be cut off, and a dressing applied exactly to the sore. The skin is usually powdered and protected by cotton wool.

Liniments must always be applied to both sides of the chest when ordered for bronchitis, and in every case should be rubbed in with the palm of the hand and not with the fingers. Painting with iodine must not be continued when smarting follows the application, unless specially ordered.

Fomentations and stupes may be made of flannel, flat sponges, spongiopiline, or lint. A convenient form is a length of flannel doubled. This is placed on a strong towel over a basin, boiling water poured over it, and the towel wrung out quite tightly; a good wringer is made by a strip of ticking sewn at both ends, and a stick passed through each. The fomentation is carried to the patient in the wringer, care being taken that it is absolutely dry. It is shaken out before application and then covered over with thin mackintosh or jaconet—at least one inch wider in every direction than the fomentation—and a layer of cotton wool, and is kept in position by a flannel binder or bandage. Such stupes may be made with a decoction of boiled poppy-heads, or be sprinkled quickly with 40 to 50 ♏ of turpentine, or 10 to 30 ♏ of tinct. opii, as may be ordered, just before application. If intended for relief of pain, they are usually changed every twenty minutes to half an hour.

In *applying leeches*, the skin must be well washed with hot water and plain (not scented) soap; antiseptic lotions should never be applied. The leech is placed in a test-tube, medicine-glass, or small tumbler, half full of cotton wool, held over the place, which should be covered with a piece of cotton wool with holes cut in it for the leeches; if the leeches are slow in biting, a little milk may be placed on the patient's skin. The leeches fall off when full, and should never be pulled off, as their teeth may be left in the wound and give rise to a troublesome sore; but if they remain too long, a little salt sprinkled on them will remove them at once. They should be handled as little as possible before being applied. Orders will be given about the amount of bleeding desirable—a warm fomentation over the bites encourages it. If to be arrested, a very small piece of cotton wool, a mere film, placed in the bite generally causes coagulation. Failing this, pressure, cold applications, or a styptic, such as adrenalin, may be tried, and the doctor must be informed. Leech-bites must be looked at from time to time for some hours, lest the bleeding begin again. The patient should not be alarmed or agitated, either in the application of the leeches or in controlling the bleeding.

Dry-cupping is done by means of cupping-glasses, or, in their place, the bowls of wine-glasses or small tumblers. A few drops of spirit are poured into one of these, and after being allowed to run over the entire surface and the excess poured out, it is set alight and at once applied.

The same effect may be produced by placing in the cup a small piece of blotting-paper dipped in spirit, lighting it, and at once applying. The edges of the glass should be previously oiled, and care taken that they do not become too hot. It is easily removed by pressing away the skin from the edge and allowing the air to enter.

Wet-cupping is performed in exactly the same manner, except that the skin is cut with a scarificator or cupping-knife before the cups are applied. After the removal of the cups, a dry dressing is applied, or a fomentation may be ordered.

Ice-bags should be half filled with small pieces of ice, and have a piece of lint or linen between them and the skin. They must always be refilled before all the ice is melted.

Ice is also applied in the form of ice compresses, which require constant changing, ice poultices, and in tubes known as Leiter's tubes, which are specially adapted for the application of iced water to the head. If the ordinary ice-bag is used for the head, it must be light, and may be tied to the top of the bed for support.

Hypodermic Injections are given, the needle and syringe being clean and the latter firmly screwed on, by first accurately filling the syringe, and then driving the fluid to the point of the needle so as to expel the air. The skin, previously cleansed, is then firmly held and raised into a fold, while the needle is gently but quickly inserted into the fold in a direction nearly parallel with the surface and directed towards the body, and pressed onward till the point has passed through the skin and well into the subcutaneous tissue; the syringe is then slowly emptied and withdrawn, a finger being placed over the puncture for a minute or two. Care should be taken to avoid any veins. If the needle is properly inserted below the skin, no bleeding or swelling will ensue. When the injection has to be made into a muscle, the skin is stretched by the left hand and the needle passed straight downwards into the limb. Great care must be taken in sterilising the syringe.

Inhalations are given in an inhaler, or in a jug with a towel placed round it so that the patient breathes only the steam. Water at 140° to 150° F. must always be used, and care taken that a weak patient does not become faint by bending over too much in a crouching attitude. The nurse should be familiar with the use of asthma powders and nitrite of amyl capsules.

A Tent and Steam Kettle are often ordered for bronchitis and tracheotomy, and can be made of folding screens covered by quilts or blankets so as to exclude all draught, and enable the space to be filled with steam. The kettle must not be too high above the patient, or in a position to allow it to drop or spurt on him; an equable temperature must be maintained, especially with young children, and the supply of steam be constant.

Purgative Enemas.—The nurse should be able to give a common enema equally well whether the patient is lying on the back or side. Generally, however, he is placed on the left side, with the

buttocks close to the edge of the bed, and the knees drawn up. The bed should be specially protected by a mackintosh and folded sheet. Restoratives should be within reach, as some patients turn faint after the enema. In this, as in douching, the washing of backs, etc., no exposure of the patient is necessary or justifiable. The nurse, having the enema ready, lubricates the nozzle of the syringe or irrigator with a little oil or vaseline, and seeing that it is full, so as not to inject air, with the forefinger of her left hand, also lubricated, ascertains the entrance to the rectum, and gently inserts the nozzle with her right hand. Great care must be taken if hæmorrhoids, fistula, or fissure be present, all of which are exquisitely tender. In cases of fæcal accumulation the nurse may be desired to break up the mass gently, with her forefinger well oiled and the nail filled with soap; she must give the enema at intervals. When this is necessary, or when there is irritability of the bowel or relaxation of the sphincters, the gum-elastic vaginal tube supplied with a Higginson's syringe is useful. It is softened by immersion in hot water, well oiled, fixed to the syringe or irrigator, and gently inserted. This tube is safer and better, as a general rule, than the short, hard bone nozzles usually supplied for rectal use. If one is not available, it is better to draw three or four inches of rubber tubing over the hard one before insertion, or to use a large soft catheter.

Simple enemas should be made with plain curd, or yellow soaps, not with the scented or medicated kinds.

Starch enemas are made by mixing from a teaspoonful to a tablespoonful of starch powder, according to the quantity required, with a little cold water into a smooth paste, and then adding boiling water until a mucilage is formed, to which the special medication is added. For a starch and turpentine enema, 1 oz. turpentine to 15 ozs. starch mucilage may be ordered; for a starch and opium, the prescribed number of minims of opium are added to the prescribed number of ounces of starch mucilage. *Castor* and *olive oil enemas* are conveniently given by warming the oil in a cup, and then placing it in a basin containing the simple enema which usually accompanies the oil. The end of the syringe is readily transferred from the water to the cup after 2 ozs. or 3 ozs. have been injected; and when the oil has been given, it is readily replaced in the water without fear of admitting air. Another method is to warm the prescribed amount of oil, introduce it into the bowel by means of a soft catheter and glass funnel, and follow it in half an hour by an ordinary soap and water enema. *Glycerine enemas* are usually given in a special syringe holding the exact amount required.

In **Rectal Feeding** it is desirable, when possible, first to wash out the lower bowel by a small enema of warm water. The quantity and materials of nutrient enemas vary according to special orders. The usual method of administration is by means of a rubber catheter, to which is attached a length of india-rubber tubing fixed on to a small glass funnel or a special glass graduated in ounces. The temperature of nutrient enemas should be 95° F.; they must be given very slowly to

ensure retention, at the rate of one ounce every five minutes, and special care must be taken that no air finds its way into the bowel. A napkin should be held to the anus for a few minutes after the tube has been removed; in all these applications great gentleness is essential.

In **Nasal Feeding** a similar apparatus to that used for nutrient enemata is generally employed. The soft catheter should be well lubricated with oil, and passed along the floor of the nose directly backwards into the gullet. Some twelve or fifteen inches should be passed, care being taken that it is really going down the œsophagus, and not coiling up at the back of the mouth. Distress or coughing indicate that the catheter may be in the windpipe, and it must at once be withdrawn and repassed. The fluid should be gently poured into the stomach in a steady stream, thus preventing the entrance of any air, which might cause pain or vomiting. When the prescribed quantity has been administered, the tube must be steadily and gently withdrawn. Passing an œsophageal tube into the stomach through the mouth is usually done by the medical man.

Baths.—In giving baths, everything must be ready before the patient is disturbed, and the temperature verified by the thermometer. In a large bath, the hot and cold water must be well mixed before this is done, and on no pretext whatever should any patient be left with the taps running. The cold water must always be turned on first, and no patient or junior assistant be permitted to touch the taps. Except in special circumstances—as in the treatment of fever, and then only by the charge nurse—the taps should never be turned after the bathing has commenced. Towels, a blanket, and if necessary a screen should be in readiness. The temperature is from 100° to 110° F. for hot baths, 90° to 100° warm, 80° to 90° tepid, and 65° to 80° cold, and the water must be tested by the thermometer during the length of time ordered. That the bath may not fall below the required degree, the water should stand a little above at first, and should be long enough in the bath to warm it through; thick stoneware baths absorb a large quantity of heat. The patient has a blanket laid over him, and as he is lowered into the bath, this remains spread across it, and is wrapped round him again when lifted out. With children the blanket may be spread over the bath first, and they are then rolled in it and placed in the bath. In giving a hip-bath the same arrangement is desirable, and a small blanket can be placed over the shoulders to avoid chill. Warm towels and wrapping in a blanket are desirable after hot baths, the bed being warmed by hot bottles. In cold bathing it is usual to lower the patient in a sheet into tepid water (90° F.) first, and to reduce the temperature by adding cold water gradually.

Special Baths.—The following are usually ordered:

(*a*) Mustard, 2 to 4 ozs. to every 4 gallons water.

(*b*) Salt, 1 lb. to every 4 gallons water.

(*c*) Alkaline, carbonate of soda or potash, 2 to 4 ozs. to every 4 gallons water.

(*d*) Sulphur, 2 ozs. to every 30 gallons water.

The time the patient remains in the bath is ordered by the medical man.

Vapour and hot-air baths can be given in bed by protecting the mattress with a waterproof sheet and blanket. The patient is stripped and placed in a blanket, with another over him. A long cradle is then placed in the bed, well covered with blankets so as to exclude all air except at the foot, where a funnel over a special lamp, or from a steam kettle on a lamp, conveys the heated air or steam into the bed. Hot drinks, such as milk or hot water, may be given with advantage to promote perspiration. A cold towel should be placed on the head during the bath. The temperature should be taken before, during, and after the bath, and the pulse felt at intervals in case of faintness. After the stated time, usually from fifteen to twenty minutes, the hot air or steam is withdrawn, the patient wrapped in hot dry blankets, and left a while before dressing him and remaking his bed.

If the bath be given out of bed, a lamp, specially protected, is placed under a cane chair, which is covered all round by blankets; the patient is undressed, wrapped in blankets, and placed on it with a screen round. The same routine is followed after the time has elapsed, except that the bed should be warmed by hot bottles.

Hot and Cold Packs are given by placing a patient on a bed similarly prepared as for the hot-air bath, and enveloping him from head to foot in a thin blanket wrung out of hot water (110° F.) for the hot pack, or a sheet wrung out of cold (65° F.) for the cold pack. If the latter be to reduce the temperature, it may need renewing after an interval, the temperature being taken in the rectum or mouth before and at frequent intervals during the process. A cold towel should be placed on the head. The patient in both cases is to be left for a time before being dressed.

Sponging is usually employed to reduce the temperature or to check excessive perspiration. It may be ordered with hot, tepid, or cold water. The bed and patient are prepared as for the vapour bath. The sponging should be light, with a sufficiently moist sponge, and always downwards, away from the body, and is usually continued from ten to fifteen minutes. In hot and tepid sponging the temperature of the water must be kept uniform during the whole process. In cold sponging it should be kept about 65° F. by the addition of ice.

Sick Cookery.—A nurse must understand the preparation of all articles of diet for the sick, and also be able to follow intelligently instructions for the diet ordered in special diseases; for example, diabetes or gout. Gruel, arrowroot, bread jelly, preparations of milk such as junket and whey, raw beef-tea, scraped raw beef (given with brown sugar in certain cases), raw meat juice, beef-tea, mutton broth, chicken jelly, custards, lemonade, barley water, etc., are all required at different times. The peptonising of various foods is also the nurse's duty, as well as giving all nourishment in the most appetising manner.

Dainty arrangements, small quantities served punctually, with as much variety as possible, and absolute cleanliness of every detail are essential. The nurse must never touch the food with her finger, blow upon it, or taste it with the patient's spoon to test its temperature. In feeding a patient who is unable to sit up, the nurse's hand, when raising the head, must be placed under the pillow. The food should be given slowly and cautiously to helpless cases, but not be dribbled ineffectually or too slowly into the mouth.

Gynæcological Work.—A nurse should understand how to arrange a patient for examination, bringing her well to the edge of the bed on her left side, the spine as nearly as possible in a line with it, the knees flexed, the right being rather more drawn up than the left, and the left arm brought round to the back, so that the patient is lying almost on her chest.

She should also know the names of the various specula (Ferguson, Sims, etc.), and be able to pass them if required. This is done by placing the first two fingers of the left hand, previously lubricated with an antiseptic lubricant, into the entrance of the vagina, and drawing the perinæum backwards so as to admit the edge of the speculum, which is passed gently in a backward direction, holding the perinæum so as to avoid touching the clitoris, or causing pain, until the os can be seen. It may be necessary to alter the position of the speculum a little, if a "Ferguson," to bring the os into view, in order to carry out special directions, *e.g.* for plugging round the cervix. The nurse must be able to prepare uterine (Playfair's) probes for use, by placing a very thin layer of cotton wool on her left palm, laying the probe at the edge of it, and, by a little manipulation and rotation of the instrument, wrapping it smoothly and firmly round. After use, the wool is removed and fresh supplied. Medicated bougies are placed in the vagina to dissolve. Suppositories are gently passed into the rectum, the finger being previously oiled.

Pessaries.—The nurse may be required to remove a pessary, and even to reinsert one. She should be acquainted with the various shapes and their uses.

In giving *vaginal douches* the nurse should protect the bed with mackintosh and folded sheet. The patient should lie on her back, with the head rather low, and a pillow under the loins. The bed-pan should be warmed before being used, and a towel be at hand. Having prepared the douche as ordered, testing its heat by the bath thermometer, the nurse places the irrigator at a convenient height above the bed and allows a small quantity of the lotion to run through the tube to expel any air. Then having lubricated the glass nozzle with sterilised oil, she inserts it gently into the vagina, unless the patient prefers to do it herself, which may be better in cases where there is great tenderness, *e.g.* cancer. The tap is then turned, the douche given, and the nozzle removed without allowing any air to enter. If a Higginson's syringe be used, the glass nozzle is easily fixed to it by removing the bone nozzle

and putting the glass into the india-rubber tube; it is then filled with lotion and inserted in the same way. The douche is conveniently contained in a jug supported at the side of the bed. Glass nozzles (without a terminal hole, lest the nurse unwittingly administer an intra-uterine douche) are the cleanest and safest, as they can be boiled and left to soak in disinfectant until wanted. If hot douches are ordered (110° F.), the vulva may be smeared with a little carbolised vaseline to protect the skin, which is often very sensitive. The bath thermometer should invariably be used, and a careful report given of the result of the douche.

Vaginal plugs and tampons are made of absorbent cotton wool, wrapped in a single layer of gauze, rolled into the required shape, and secured by linen thread. Tampons are pear-shaped, with the thread attached to the lower end, and are generally used for applying medications to the vaginal walls. Plugs may be made by turning in the edges of a square of wool, and forming it into a sausage-shaped roll secured in the middle by a long thread. For supporting the uterus and packing round the cervix several of these rolls are attached to one string, forming the "kite-tail" plug. For plugging through a speculum, rounds of cotton wool of varying sizes, with the thread passed through the middle, or strips of medicated gauze or lint are convenient. In every case the thread should be long enough to be well beyond the vagina, and the exact number of plugs inserted noted down.

In *passing the female catheter* the patient should lie on her back with the knees drawn up, though in some cases, such as ruptured perinæum, the left side is better. The vulva must first be thoroughly cleansed with warm water, and also all the parts round the meatus, with a disinfectant, 1 in 4000 perchloride or boracic lotion, applied with wool sponges. The catheter may be gum-elastic, flexible india-rubber, glass, or silver. It must have been boiled for five minutes and kept in a solution of 1 in 2000 perchloride or 1 in 20 carbolic acid, and washed with sterilised water. The eye must be perfectly smooth. It is lubricated with sterilised oil, and the nurse, having previously disinfected her hands, holding it in one hand, with the index-finger of the other finds the entrance to the vagina. Just above this the hard round meatus urinarius (with its depressed central orifice) is easily felt, and the catheter passed into it, the other end being placed in a convenient receptacle. If there be much vaginal discharge, or the nurse cannot pass the catheter into the orifice at once, the catheter must be boiled again or another one used, and the nurse must ascertain the position of the meatus by the eye, and insert the catheter. It is most important that no discharge should be carried into the bladder, there being great danger of cystitis if the strictest cleanliness is not observed. Any marked tenderness in passing the catheter must be reported, as it may be due to urethral caruncle or other special cause. In cleansing the catheter a strong stream of water must be run through it from the eye, and it then must be boiled and placed in a disinfectant.

In *washing out the female bladder* the catheter is passed in the usual way, and the urine drawn off. The nurse has ready in a jug the prescribed quantity of the warm lotion to be used (frequently boracic), and an india-rubber tube about one yard long, to which is attached a glass funnel holding 4 ozs. to 6 ozs. The free end of the catheter is placed in the tube, which the nurse compresses a few inches above the catheter between the second and third fingers of her left hand, holding the funnel between her thumb and index-finger. With the right hand she fills the funnel and tube from the jug, and then, releasing the tube and raising the funnel, she allows the lotion to flow into the bladder, compressing the tube again just before the funnel is empty. After repeating this once, or even twice, she removes the tubing from the catheter and allows the bladder to empty itself. The tube is then readjusted, and the process repeated until the prescribed quantity of lotion has been used. A glass measure should be at hand to receive the contents of the bladder, and to ascertain that no lotion, or only the specified amount, is retained. The nurse must carefully examine the catheter lest the eye become blocked by mucus, as is often the case in cystitis.

The **Nursing of Children** calls for special watchfulness, and that keen and sympathetic power of observation which can distinguish between fretfulness and pain, hunger and temper, caprice and loss of appetite. In nursing fretful children kindness is essential, and it need scarcely be said that corporal punishment should never be thought of.

One very common error is moving sick children about too much. A nurse who would not dream of unnecessary exertion for an adult with acute bronchitis or pneumonia, will not realise there is harm in raising a child similarly affected into a sitting position to change linen, poultices, and so forth; and will even take it out of bed to wash it on her knee by the fire, forgetting that if easy to her to lift and move a child, it by no means follows that it is easy to the child. Sick children should be handled as nearly like adults as possible. Special care is necessary to keep them dry and clean; they should be attended to every two hours by day, except when sleeping soundly,—when four hours may elapse,—and twice at least during the night. Attention after each meal is desirable, and habits of regularity taught as far as may be. Careful washing and powdering are essential. Flannel night-gowns made long, which may button below the feet, prevent chill when a restless child throws off the bed-clothes in its sleep. When dressing wounds, the child's attention should be diverted as much as possible, half its crying being from fright rather than pain. Children should never be deceived with regard to pain, the taste of medicine, and other unpleasant experiences; if they find they have been told what is untrue, the power of the nurse is gone.

Children must be induced to take the amount of nourishment ordered: firmness and kindness go far in attaining this. When, in whooping-cough, food is rejected from the stomach, it is well to give more as soon as a paroxysm is well over, to ensure that some be assimilated before the

next fit of coughing. A bath when ordered in convulsions ought to be from 90° to 95° F., deep enough to immerse the child up to the neck, and the temperature kept equal by adding more hot water from a can, not from a tap; a blanket is thrown over the bath, and cold or iced applications placed on the head.

In **Ophthalmic Nursing** the nurse is trained in the use of the various applications prescribed. She should be able to evert the eyelids easily, a simple but by no means generally understood process, best accomplished by turning the upper lid backwards over a probe, while the lower lid is drawn downwards, the patient at the same time looking in a downward direction.

In **Infectious Diseases** much responsibility devolves upon the nurse. Isolation of the patient and the thorough disinfection of all that pertains to him are most important. It is usual to keep a sheet wet with 1 in 40 carbolic acid lotion hung over the door of the sick-room. All body linen and whatever has been worn by the patient should be immersed in 1 in 40 carbolic or in 1 in 100 solution of izal or lysol at the bedside, and should not be first carried down the ward or out of the room.

In dealing with *linen soiled with excreta*, especially in cases of enteric fever, it should be rinsed with plain water, and then placed in the disinfectant. Such linen should soak for twelve hours at least, and, if possible, be boiled before going to the laundry. Handkerchiefs should never be used in cases of scarlet fever, measles, or diphtheria, nor, if possible, in pulmonary tuberculosis. The best disinfectant for excreta is chloride of lime, but the use of this is not always possible on account of its strong smell. One in 20 carbolic or 1 in 50 izal may be used, but in all cases the stools should be exposed to the action of the disinfectant for four hours before being disposed of.

The urine of an enteric patient should be similarly treated. All discharges from the patient's nose and mouth should be wiped away with wool and destroyed as soon as possible, and 1 in 20 carbolic or 1 in 1000 perchloride should be placed in any cup used for the reception of sputum.

The nurse must take a carbolic bath, not forgetting her hair, change every article of clothing, have all garments worn in the room disinfected, and, if possible, have some days' interval before returning to work. After a case, the room and all belonging to it must be thoroughly disinfected, and also the rooms of all those who have been in attendance on the patient. All cups, glasses, knives, should be boiled. All small articles that can be spared should be destroyed by burning. All bedding, curtains, carpets, blinds, etc., should be sent to a disinfecting station to be treated with steam whenever possible. If this cannot be done, they should be thoroughly fumigated and then exposed to the open air for some time. The room is best fumigated by means of formalin or sulphur; after the latter the walls should be stripped and repapered, the ceiling whitewashed, floors and all woodwork washed with disinfectant, and, if possible, repainted.

The nurse in attendance on infectious cases must never eat in the room, must cleanse her hands thoroughly after contact with the patient, and, especially in cases of diphtheria, should rinse the mouth and gargle with a disinfectant at intervals.

In *scarlet fever* the nurse is frequently directed, in addition to warm baths, to anoint the patient all over during the process of desquamation.

In cases of *diphtheria* the nurse must hold herself in readiness to prepare the patient for the injection of antitoxin, and to report the results. Its use is sometimes followed by a rash. Absolute rest is essential for a diphtheria patient, to diminish the risk of cardiac failure.

In cases of *tracheotomy* the temperature of the room must be kept perfectly equable. A steam tent may or may not be required. If ordered, the moisture must never fail, and the temperature be kept from 70° to 75° F., as tested by a thermometer hanging inside the tent. A moistened fold of gauze should be kept over the mouth of the tube, and frequently renewed, the piece removed being burnt immediately. All instruments needed must be kept close at hand. If feathers are ordered, they must be carefully selected, sterilised, and burnt directly after use. The nurse must understand cleansing and changing the inner tube; also how to replace the outer one in an emergency, or, if this is impossible, to keep the tracheal incision open with the forceps until the doctor can arrive. Such cases should be fed in small quantities at frequent intervals; if there is any difficulty in swallowing fluids, orders may be given to thicken the milk with arrowroot or corn-flour, or to give milk-jelly ($\frac{3}{4}$ oz. of isinglass to 1 pint milk), beef-tea jelly, or plasmon and milk jelly—or nasal feeding may be required. Intubation may take the place of tracheotomy. The nurse must keep the patient lying on one side as much as possible, and frequently swab out the mouth to remove the mucus which comes up the tube. Feeding must also be managed with the patient lying on the side to enable the food to pass the opening of the tube. Should the latter become blocked, the nurse must remove it by loosening the string and pulling on it in an upward direction. She must at once send for the doctor.

Nursing of Patients with Pulmonary Tuberculosis.—Nurses are often required to assist in the open-air treatment of phthisical patients. Tact and sympathy are necessary in dealing with phthisical patients to persuade them to carry out the prescribed treatment. Every precaution must be taken to disinfect the sputa, which, after being collected in a special receptacle containing disinfectant, should be burnt. Every room occupied by a phthisical patient, especially when in the last stages, should be thoroughly disinfected.

Private Nursing.—This branch of the profession affects the general public more closely than any other, as both doctors and patients depend almost entirely on the trustworthiness and experience of the nurses; and yet it is the one most open to women of little or no pretensions to knowledge. That this is possible is due to the ignorance of the community at large, the apathy and mistaken kindness of medical men, and the cupidity

of speculators. When women can be engaged at low salaries, with little or no investigation of their antecedents, and sent out as "trained nurses" at fees calculated to yield a handsome profit, who can wonder that the results are unsatisfactory to all concerned?

The manner and dress of a nurse serve as guides to the thoroughness of her training. A woman who is scrupulously neat, in a suitable inconspicuous uniform, business-like in manner, yet bright and pleasant, who takes her orders quietly yet intelligently, and who keeps strictly to her own position, is likely to be suitable. Nurses need a "professional" manner as much as medical men, and the latter would add to the dignity of both professions by recognising and encouraging the fact. Flippancy and familiarity are especially unworthy of those whose work involves such grave responsibilities. Mutual respect is the groundwork of the confidence which must exist if the patient is to receive the full benefit of the treatment. The medical man must feel able to trust the nurse's ability and trustworthiness in carrying out his instructions to the smallest detail; and the nurse must prove herself deserving of such trust, and add to her other duties an absolute loyalty towards the doctor. By her manner of obeying orders she can also inspire the patient with wholesome confidence. If at any time the nurse cannot be present at the doctor's visit, a *written report* must be left for him, and his orders for her should also be in writing, so as to avoid any misunderstanding. Orders should be given directly to the nurse, not through the friends; and care taken that she really understands them. Her report also should be given to the medical man, if necessary, before he sees the patient, or after, if not desirable in the sick-room.

The nurse should never take friends into confidence about the case, nor express her own opinion to them. Infinite harm is done in this way, and often remarks are quoted to the medical attendant in a different manner from that in which they were originally made. The vice of gossiping is a very grave one, and unfits a nurse for her office almost as much as the vice of intemperance. If a woman persists in thus offending, she should not be employed. Criticism of medical treatment, suggestions of further advice, or even of a change of the medical man, should never be tolerated; such behaviour is unconscientious in the highest degree, opens the door to suspicions of touting for special doctors, and might lead to the gravest results to the patient. If a nurse cannot conscientiously continue to work for a medical man, she must have the courage of her convictions, and leave the case without reflecting on him in any way.

When sending for a nurse, the medical attendant can do much to put her on a right footing with the household she is to enter. Too often training is supposed to render a nurse indifferent to sleep, exercise, or regular food. It should clearly be explained that eight continuous hours for sleep, at least one hour for exercise, and time for each meal are necessary as a rule, though a good nurse will make exceptional efforts in case of emergency. Her meals should not be served in the sick-room; and if on night duty, her bedroom should be in a quiet part of the house.

Necessary sleep and exercise are essential to keep a nurse fit for the duties and responsibilities which devolve upon her. The doctor generally knows something of the household, and can give the nurse some valuable hints which may enable her to avoid friction.

A private nurse needs special neatness and refinement, so as to keep both the patient and his surroundings in pleasant order. The toilet of the patient calls for scrupulous nicety; nails, hair, etc., being carefully attended to. The housemaid's work will depend upon the domestic arrangements, and is generally done by a servant, but the nurse is responsible for the room being in order. She can do much to comfort her patient by avoiding all unnecessary noise in remaking the fire (using housemaid's gloves to lift the coal, which should be in lumps); shading his eyes from too strong light, whether from lamp or window; arranging flowers; finding out any particular like or dislike, and, if possible, attending to it; avoiding all whispered conversations, creaking doors or windows, flapping blinds, creaking shoes, rustling or rattling dress or ornaments; not shaking the bed in passing—in fact, feeling with as well as for the patient. When her services are not needed, the nurse is better out of the patient's sight, though close at hand; and this is especially desirable if the nurse be reading, as in some long night-watches she may, lest she sleep; needlework is seldom resented by a patient. A nurse should invariably wear her uniform when on duty, whether by day or night, unless there are special reasons for not doing so.

Much depends upon the way in which the nourishment is presented, as to whether the patient will take it or not. This is entirely the nurse's province, and her knowledge of sick cookery should supply any deficiency in this respect in the household. Everything should be served as daintily as possible—glasses, spoons, etc., perfectly clean and polished, clean tray-cloth, if possible a few flowers, small portions, and any particular fancy as to sweetness remembered. Every particle of fat should be removed from broths and beef-tea, toast should be thin and crisp, bread and butter thin and lightly spread, nothing spilt on plate or saucer. The patient should not be told, as a rule, what is coming, as food when unexpected is often more readily taken. Rigid punctuality is necessary; nothing spoils an invalid's appetite like delay. No stimulant should ever be given or allowed without direct medical orders, and the kind and quantity must be entered in the diary. Food should never be kept in the sick-room, and plates, glasses, etc., should be removed as soon as possible. Ice will keep much longer if wrapped in flannel and placed on a colander to let the water drain away.

Arrangements for *operations* are carried out by the nurse in the best way allowed by circumstances. The room should have as little superfluous furniture as possible; if the carpet cannot be removed, it should be well swept, and wiped over with a disinfectant lotion, which latter process should be repeated daily. The operating table should be in a good light, firm, narrow, and thoroughly clean; it is often better to have two narrow tables placed end to end. It is usually covered by a double

blanket, a mackintosh sheet, and a clean sheet. A small pillow, and a blanket to cover the patient, are also needed. There must also be tables for the use of the surgeon and his assistants, and a chair for the anæsthetist. Plenty of hot and cold water (the latter previously boiled), basins, flat dishes for instruments, towels (sterilised by boiling), the prescribed lotions, and stimulants must all be at hand, as in hospital practice.

Infectious cases are comparatively easily managed in a private house. A nurse needs great tact in so dealing with the friends and relations that orders may be carried out without offending them. If in any difficulty they will not yield to her persuasions, she must appeal to the doctor for advice. Thoughtfulness for their natural feelings, and also for the household arrangements, to avoid giving unnecessary trouble, will do much to promote friendly relations. Half the troubles that occur are due to the nurse's inexperience in adapting herself to the altered conditions in which she has to work; it needs both tact and disciplined training to enable her to adjust herself satisfactorily to the new circumstances.

District Nursing.—Nursing the sick poor in their own homes is now a recognised branch of the profession, though it is not equally realised that this work requires specially trained women. The cases are as varied and critical as any to be met with in hospital or private work, with none of their favourable surroundings. In many places—manufacturing centres, for instance—where the population has rapidly outgrown the hospital accommodation, or in scattered country districts, where the nearest hospital or infirmary may be many miles distant, the most serious cases must perforce be nursed at home. There are innumerable instances where removal would probably cause a fatal termination to the illness, and is only attempted as a lesser evil than leaving the patient to suffer untended. If a parent, especially the mother, is removed to hospital, the whole family may be broken up, and the worst moral results ensue. Where there are young children, also, the anxiety about them in her absence is a serious drawback to the mother's recovery. There are also many cases unsuitable for hospital, such as chronic rheumatism, paralysis, cancer, phthisis, children with hip and spine disease, who can perfectly well be attended in their own homes by a trained nurse. It has a good moral effect in many cases for children thus to support aged parents, or for brothers and sisters to keep a delicate member of the family at home, instead of sending them into the Poor-Law infirmaries at the expense of the ratepayers. A district nurse, therefore, needs full hospital experience if she is to carry out medical orders efficiently, and in addition requires special training to meet the difficulties of the work. Ignorance, prejudice, dirt, foul air, and often want of the commonest necessaries have all to be met; and nursing knowledge alone is of little value if it cannot be used to the best advantage in the circumstances. Still less can a woman who has only given three or six months' time to acquire both nursing and district experience prove a thoroughly satisfactory district nurse.

The usual method of work is for a nurse to have a certain number of cases within reasonable distance under her care, which she visits once, twice, or even oftener every day, taking entire charge of each patient with regard to washing, bed-making, changing linen, applying poultices, dressing wounds, etc. She is also responsible for the sick-room and all its appliances being kept fresh and sweet, and as far as possible in a cleanly, tidy condition. It has been objected that unless the nurse remains with the patient no real good can result from her attendance. In a critical case, where constant skilled care is essential, arrangements can be made for the other patients so as to enable the nurse to devote herself entirely to one for a time. But it is a district nurse's duty to teach the friends the right way to wait upon the sick person. They are generally anxious to help, and a sensible man or woman can be educated to be an intelligent assistant, who may be trusted to administer nourishment and medicine at the proper intervals between the nurse's visits.

No nurse, however well trained, should be expected or allowed to treat or prescribe for any case beyond rendering first aid in emergencies. She should never undertake the nursing of a case that is not under a medical man, nor initiate or alter any treatment without his direct orders or permission; as in private work, all suggestions, criticisms, and discussions of his methods are utterly inexcusable. Gossip is, if possible, a more fatal fault in district than in private work. Besides not talking of one patient to another, the nurse should be reticent concerning her cases to those above them in the social scale. The respectable poor resent their private affairs being made known to district visitors, committee ladies, etc., and a nurse who thus betrays confidence will lose all influence over her patients and their friends.

A district nurse is generally sent to cases by medical men, clergymen, district visitors, or the friends of the patient. If not sent by the medical man, it is more courteous for the nurse to ask his permission before going to the case, though she might help the friends to carry out orders at the first visit, and then ascertain if he wishes her to continue. A *written daily report* should be left for the medical man,—in acute cases twice daily, or even oftener,—with the record of the temperature, pulse, respiration, action of bowels and bladder, amount of sleep, food, stimulants, etc. In chronic cases an occasional written report may be sufficient, stating the general state of health and any special observations. By thus keeping in full communication with the doctor, mistakes and misunderstandings are avoided. Many difficulties would be saved by one rule, viz. that both doctor and nurse *invariably* communicate in writing, never giving or receiving verbal messages from patients or their friends. By implicitly carrying out medical orders, and by exact obedience, the nurse will impress the friends with the importance of obeying directions. She must aim at being the friend, not the supplanter, of the wife or mother, who may resent a stranger's intrusion until experience teaches how much more can be done by skilled hands. It is generally much easier to put the patient than the room in nursing

order. But by degrees the most disorderly room can be arranged, and whenever possible this should be done, not by the nurse personally, but by the friends acting on her advice. The lesson is more permanent if they realise themselves that they can make and keep things tidier and more orderly. They prefer themselves to put away the extra garments that have accumulated, to remove the family linen "airing" between the bed and mattress of the sick person, to clear out boxes, sacks, and other rubbish that may be under the bed. If, however, no one else be available, the nurse must ensure cleanliness herself, for she is responsible that all the appliances and surroundings are in order. She must be prepared to extemporise many kinds of contrivances. If it be not possible to move the bed from a draughty position, a screen can be made from a clothes-horse and a shawl, if a quilt or blanket is not available; or the same garment may be fastened as a curtain on a clothes-line. A roll of newspaper or brown paper will convert a common kettle into a steam one for the time. A sheet of the latter material is an excellent temporary substitute for mackintosh. A small teapot forms a good feeder, a chair can be converted into a bed-rest; in fact, a good district nurse is rarely nonplussed for ways and means.

A stock of the necessary appliances, such as water-pillows (more generally useful than the large water-beds), mackintoshes, bed-pans, etc., should be kept for lending; also sheets, bed-garments, etc. Flannel shirts, open down one side, are particularly useful for rheumatic cases. A free use of Keating's powder, carbolic acid, or Jeyes' fluid for bedsteads, floors, etc., with carbolic soap and turpentine, are useful in diminishing insect life.

Except under special circumstances, night duty is the exception for a busy district nurse, as it prevents other work. Trustworthy women, working under orders, can generally be found to relieve the friends at night.

The nursing of infectious cases depends entirely upon the local medical men. Except in epidemics, scarlet fever, diphtheria, and measles are not usually attended by the nurse. With due precautions, most careful disinfection of hands and instruments, and the use of separate sleeves and aprons, enteric fever, whooping-cough, and erysipelas may be attended without risk to other patients.

Care would necessarily have to be taken not to go to another child after visiting whooping-cough, nor to a surgical case when attending erysipelas; but ordinary chronic adult cases and acute diseases such as rheumatic fever and pneumonia may easily be nursed at the same time.

District nursing should be entirely distinct from any form of almsgiving. All relief should be obtained from the proper local sources, never given directly by the nurse. Also the work should be unsectarian if it is to reach those most in need of its help.

The founding of Queen Victoria's Jubilee Institute for Nurses for the Sick Poor, by her late Majesty Queen Victoria on the occasion of the celebration of the fiftieth year of her reign, has systematised the most

favourable conditions for carrying out district nursing. "Queen's Nurses" must hold a recognised certificate of hospital training, and receive six months' special training in the homes of the poor before starting work in a district. They are periodically inspected from the Queen's Institute, and work under specified conditions accepted by the associations employing them. To meet the requirements of country districts where neither work nor funds justify the engagement of a fully trained nurse, County Associations have been formed. Their object is to supply scattered rural districts with women of the county specially trained in midwifery and maternity nursing, and with some knowledge of the care of the sick. In County Associations, affiliated to the Queen's Institute, these village nurses are under the supervision of a Queen's Nurse who is also a midwife.

When arranging for a district nurse in any locality, it is useful to obtain information respecting these various systems. A lay committee often meets with many difficulties from want of experience in organising a successful association.

The arrangements as to midwifery being taken by district nurses are made by each association to suit local needs. It is increasingly desirable that, whether practising or nor, district nurses should be registered midwives, in view of the emergencies that arise, especially in country work.

Whenever possible, it is desirable to let the people of a district help to support the nurse. This may be arranged on the lines of a provident club—a monthly payment of 4d. per family (or 2d. if local wages are low), with a similar charge of ½d. or 1d. per head for adult wage-earners, is not a heavy tax, and fosters a desirable feeling of independence. In manufacturing or mining centres the workers will agree to a small regular deduction from their wages for the same object, and a house-to-house collection brings the work to the notice of all and removes any feeling that the nurse's services are a charity. The only exceptions are patients in receipt of Poor-Law relief, who could not contribute to any fund; but the Boards of Guardians (under the Local Government Board Standing Orders, 42 and 43 Vict. cap. 54, sec. 10, and Circular issued under date Feb. 1, 1902) are empowered to make grants to district nursing associations.

Monthly Nursing.—Although the puerperal state is naturally a normal one calling for little beyond cleanliness and ordinary attention, grave complications may arise from constitutional or accidental circumstances. It is desirable that nurses undertaking this work should be registered midwives. Not only will the wider experience be valuable should delivery take place before the arrival of the doctor, but the more competent the nurse the more she realises and prepares for any difficulties that may arise. Under the Midwives Act (1902), registered midwives are allowed no responsibility unless the conditions of mother and infant are normal in every respect. At present it is a "counsel of perfection" to require that midwives and monthly nurses should also

have general training, but whenever the further knowledge is available it adds greatly to the comfort and well-being of those under the nurse's care.

Absolute cleanliness is the secret of successful monthly nursing. A nurse attending confinement cases should always wear dresses of washing material, large white aprons, and sleeves that will turn up above the elbows. She must be scrupulously clean in person ; her hands especially must be free from roughness and scratches, with short nails kept absolutely clean. Her hair should be frequently washed and neatly arranged. She should be quite free from any wounds or sores ; many a case of puerperal septicæmia might have been traced to the unsuspected ulcerated leg of the old nurse in attendance.

The nurse's duty is to prepare the patient and bed, to have all in readiness for the infant, to wait upon the doctor, to put mother and child comfortably back to bed when all is over, and to nurse the case under medical orders. It is advisable for her to ascertain beforehand if her patient has the necessary appliances, so as to avoid confusion at the time. The room should be bright and cheerful, as quiet as possible, not near any closet or sink, and easily ventilated. The bed should be in such a position that it can be approached on both sides. The fire should be lighted, plenty of hot and cold water (which has been previously boiled) in the room, two or three basins, a quart jug (in which to warm forceps if needed), a slop pail, towels, napkins, infant's clothes, dressing for the cord, dusting powder, sterilised olive oil, threaded needles, thimble, safety-pins, blunt-pointed scissors, sterilised thread ligatures, flannel receiver, antiseptic lubricant, flannel, plain soap, etc. If possible, sanitary towels should be used for the patient; if not, ordinary diapers should be boiled before use.

Brandy, hypodermic syringe, irrigator, Higginson's syringe, sterilised glass nozzle and catheter, and a receiver for the placenta should be at hand.

Preparation of Bed.—A convenient arrangement of the bed is made by spreading a mackintosh sheet over the mattress, covered by a blanket and under-sheet. In district cases sheets of strong brown paper will serve as a temporary mackintosh. Over the under-sheet another piece of mackintosh is laid, covering the lower half of the bed on the right side. This is covered by a small blanket, a folded sheet, and, if procurable, an accouchement sheet. In poor homes, clean old quilts or any thick material can be used over brown paper, or an oilcloth table-cover. The bed-hangings should be moved from the side of the bed. The mackintosh, etc., may be kept in position by safety-pins at each corner. The upper-sheet, blankets, and quilt are folded back to the left side of the bed, ready to be replaced, and a sheet or small blanket, as preferred, is placed over the patient. A clean draw-sheet and the binder are rolled up and placed in readiness, with six strong safety-pins. A pulley is firmly fastened to the foot of the bed (an ordinary round towel is useful for the purpose), and if necessary a piece of board is placed against the foot-rail for the patient's feet.

Toilet of Patient.—She is dressed in clean night-clothes, turned up and secured on each shoulder by a safety-pin. A couple of clean petticoats may be worn, one of flannel, stockings without garters, bedroom slippers, and a dressing-gown, which latter garment is removed and a shawl put across the shoulders when the patient has to lie in bed.

The nurse should recognise the stages of labour by the pains, the short "grinding" ones of the first being distinct from the propulsive "bearing down" ones of the second.

First Stage.—If the bowels have not been well relieved, a small soap and water enema may be given in the first stage, especially if the membranes have not ruptured. The patient should also be directed to empty the bladder. She should be encouraged to walk about, and to take food, usually warm milk or beef-tea.

The nurse must be prepared for vomiting during the first stage of labour; and sometimes a shivering fit, without any rise of temperature, announces its termination.

The nurse should always thoroughly cleanse her hands with hot soap and water and nail-brush, and then immerse them in 1 in 1000 perchloride lotion before touching her patient; and it is well for her to keep a basin of antiseptic lotion at hand, so that she may dip her hands in it each time she attends to the case.

Second Stage.—When the pains become decidedly propulsive, the patient must lie on her left side with her spine in a line with the edge of the bed, her head supported by a pillow or pillows, the knees flexed, and the feet pressing against the foot of the bed. The nurse can materially assist the patient at this stage by supporting the lower part of the back during each pain. She may be ordered to apply hot fomentations to the perinæum if there be rigidity; these consist of wool or flannel wrung out of hot antiseptic lotion, and must be frequently renewed. When the child is born, the nurse should hand scissors and ligatures to the doctor, and, if desired, hold the uterus while the child is being separated. A small basin and pieces of wool will also be ready for the doctor to bathe the infant's eyes with the prescribed lotion. She has the flannel receiver ready warmed, in which she wraps up the infant, and puts it away in a warm place. If animation be suspended, she must quickly prepare basins of hot and cold water, and help as directed with artificial respiration, rubbing with brandy, dipping into hot and cold water, etc. After the expulsion of the placenta, the nurse will take the orders of the doctor as to when the mother is to be made comfortable; this is generally done after the child has been dressed.

First Toilet of Infant.—The temperature for the infant's first bath should be from 95° to 100° F.: the child is quickly soaped, placed in the water, and gently, yet firmly, rubbed to remove all the adherent deposit from its skin, and is carefully dried, especially in the folds of the skin. Until the meconium ceases, oiling the buttocks and thighs will be found useful. Before dressing the cord, the ligature must be carefully examined, and if not firm, or there be oozing, it must be re-tied; the

genitals and anus should also be examined, so as to detect any malformation. The cord may be wrapped in antiseptic gauze, or it may be well powdered with a mixture of equal parts of oxide of zinc, starch, and boracic powders, and enveloped in sterilised linen. This is kept in place by the flannel binder, which should be firmly but not tightly applied. *No pins* must ever be used to fasten the several garments; they must be neatly sewn on, except the napkins, which are secured by a safety pin, and the ends of the long flannel, which are turned up over the feet, are similarly secured at each corner. If the infant be feeble or premature, the bath may be dispensed with and the child rubbed with warm oil and wrapped in cotton wool.

Toilet of Mother.—When the child is dressed, the mother, having rested, is made comfortable. The vulva, thighs, and buttocks are thoroughly cleansed from every particle of discharge, well dried, and warm sanitary towels applied. Hot soap and water may be used with advantage, followed by a quick sponging with hot 1 in 4000 perchloride or other disinfectant lotion. The soiled draw-sheet and mackintosh are rolled tightly up against the patient, who turns towards the nurse on to the clean draw-sheet, also rolled close to her. The soiled sheet is drawn away, the other side of the patient washed and dried, the clean sheet spread out, an accouchement sheet placed in position, and the patient turned gently on to it. She lies on her back with the legs extended for the binder to be applied.

Application of Binder.—When this duty falls to the nurse, she puts the rolled-up strip of material, which is better than any shaped band, under the patient, bringing one end across the abdomen, so that the ends overlap in a line with the right hip. The lower edge should be well below the great trochanter, and the ends pulled tightly together, the left hand holding the under, the right hand the upper side, securing them by a strong safety-pin. This is repeated until the whole abdomen is firmly bound, and at the last pin a fold is made in the under side of the binder to make it fit better, and it is left rather looser to avoid compressing the ribs. Two people then gently lift the patient to the top of the bed; one raises the buttocks by grasping both sides of the draw-sheet, while the other raises her head and shoulders. Only one pillow is necessary at first. The night-dress is unpinned from the shoulders and drawn down, the covering blanket removed, the bed-clothes replaced, and the child given to its mother.

The *pulse* should be taken, also the temperature; any rise above 100 in the pulse should be reported at once, and the nurse must be on her guard for hæmorrhage. The placenta is placed in clean cold water for medical examination, and then is burned by the nurse.

Tidying of the Room.—All soiled clothes must be removed from the room as soon as possible, and put to soak in cold water containing carbolic or other disinfectant. The room must be kept quiet, and the patient left to rest. Nourishment will be as ordered, but usually warm milk, egg and milk, or a cup of tea with much milk in it, are allowed

almost at once. The nurse must obtain full instructions from the doctor as to douches, use of the catheter, record of pulse and temperature, and so forth. The room must be warm, well ventilated, and the patient remain quiet for the first week.

After-care of Mother.—She must be kept scrupulously clean, the vulva being bathed at least twice daily, and after micturition or an action of the bowels. Douches will be given as ordered by the doctor—in every case the bed-pan, sanitary towels, sheets, night-dress, etc., should be warm when given to the patient.

The diet is usually light until the bowels have acted, and then ordinary digestible food may be given. Stimulants are never to be given without orders. It is wise for her to avoid cheese, pickles, uncooked vegetables while suckling, as they are apt to disagree with the child.

The nipples must be well bathed and carefully dried before and after suckling, and the breasts should be alternately relieved. If the nipples become tender, the doctor must be informed, as special applications, such as glycerin and tannin, eau-de-Cologne and water, or a nipple shield may be ordered. The child should never be allowed to go to sleep with the nipple in its mouth, as this is a fruitful source of cracks and tenderness. If the breasts are very full and tense, with more milk than the child can take, they may be supported by a binder, and the breast-pump may be ordered. If hardness still continue, hot fomentations and support should be applied until the doctor has seen the breast; the nurse must never use friction without instructions.

Should a mammary abscess form, the breast must be well supported by a spica bandage; usually the patient's arm is fastened to the side. A convenient support, if poultices or fomentations are ordered, is a square of linen with tapes at each corner, two of which tie round the waist, and the other two round the neck, holding up the breast. The square may be folded to fit the breast, and secured by a safety-pin.

Torn Perinæum.—If the perinæum has been torn and stitched, the nurse may be directed to pass the catheter for some days, and this should be done as the patient lies on her side, to avoid stretching the parts. The wound needs constant care to keep it as clean and dry as possible, the dressing being frequently changed. If douches are given, the tube must not touch or rest upon the lacerated part. The binder should be put on as low as possible, and the knees tied together, the patient being kept strictly recumbent.

If allowed to micturate naturally, the patient should lie on her face, and the parts must be well bathed directly afterwards.

White Leg.—Should the patient complain of pain in the calf or thigh, the limb must be kept perfectly quiet until the doctor comes. If the pain be severe, hot wool may be applied, but no friction or movement of any kind attempted until orders are received for treatment. A cradle should be placed over the limb to take off the weight of the bed-clothes, and the patient must be moved as little as possible—special attention is to be paid to the back, ankles, etc., as sores are very liable to form. The

patient must never raise herself suddenly, or sit up while the leg is affected. Should shortness of breath occur, the doctor must be summoned at once, the patient kept as quiet as possible, and a stimulant given.

Should *septicæmia* arise, the nurse's duties are similar to those in a a case of peritonitis. Any abdominal tenderness, offensive lochia, scanty flow of milk, or rise of temperature must be reported at once. A strict course of disinfection for the nurse, and for every garment and appliance taken by her into the house, must be carried out. She must obtain permission from the medical man before attending another lying-in case.

The Infant.—Much depends upon the nurse in training an infant in regularity of feeding and sleeping; if this is effected, both mother and child benefit. The baby should not sleep in the bed with the mother, but in a cot at the side, and should be kept warm by hot bottles. Among the poor, many infants are killed by suffocation for lack of this precaution. A daily bath at a temperature of 90° to 95° should be given. The eyes should be thoroughly cleansed every day with warm water; any redness or discharge must be at once reported, and the lotion ordered applied. A separate piece of wool or soft linen should be used for each eye, and burned at once, while soft linen is employed for cleansing the mouth and nostrils. The mouth should be washed after taking the breast. The cord is dressed daily, and, after it separates, a folded pad of linen should be applied to the umbilicus for a few days. If the navel be inclined to protrude after the cord has come off, the doctor may order a counter, covered with lint or linen, to be fastened over it with a strip of strapping 2 inches wide and 4 long, under the flannel binder. If the bowels and bladder are not relieved within twelve hours after birth, the doctor must be told; a hot bath will often have the desired effect. After the stools become yellow in colour, any green motions, stools containing curdled milk, constipation, straining, or distension of the abdomen must be reported. Constant cleanliness and dryness are necessary, and care should be taken that the napkins are not washed in soda and water, as this chafes the skin. Any rash, sore, discharge, or persistent snuffling must be reported at once. If the child's breasts become tender and swollen, they must be protected from pressure by a piece of wool and shown to the doctor. The nurse must never squeeze or rub them.

No stimulant or medicine should be administered to mother or infant without orders, except in an emergency. Warmth and dryness keep a child contented; many an attack of screaming attributed to "wind" is really due to cold feet. In obstinate flatulence dill-water may be ordered, and a small teaspoonful of warm olive oil relieves constipation.

Clothing.—The binder and clothing should never be tight, or both digestion and circulation suffer. Light warm garments, especially knitted woollen vests with long sleeves, should be recommended, and the use of gowns with low necks and short sleeves discouraged.

Feeding.—It must not be forgotten that as the stomach of an infant can hold but a small amount, from 1 oz. to 1½ oz., overfeeding induces

flatulence and vomiting. If suckled, the child is put to the breast from time to time until lactation is established. If it seems very hungry before this occurs, it may be given a teaspoonful or two of milk and water (one of milk to three of water), warmed and sweetened. After the milk has come, the infant should be suckled every two hours during the day and every four during the night for the first fortnight or three weeks, gradually lengthening the intervals, especially at night.

If artificial feeding becomes necessary, the nurse is responsible for the preparation of the prescribed food. This is usually cow's milk mixed with boiled water or barley-water, warmed (temperature 95° F.) and sweetened. Cream may also be added. Other preparations may be necessary, such as "humanised" milk, or special foods, all of which the nurse must understand.

The bottles must be scrupulously clean—the boat-shaped are the best, and Timpe's (according to Professor Escherich) possess the advantage of having inscribed on the glass a scale of quantities to be prepared daily in proper proportions, and the amount for an infant's meals from three days old to twelve months. Two bottles should always be in use; one, well scalded with hot soda and water, and rinsed in cold water, is left in boracic lotion until needed, when it is washed out with hot water before being used. The hole in the teat should not be too large, and tubes should be cleansed each time with a brush, though it is undesirable that this kind of bottle should be used at all. Much can be done by an intelligent and tactful nurse in the instruction of mothers in the important subjects of the proper feeding and clothing of young children.

AMY HUGHES.

THE HYGIENE OF YOUTH

By CLEMENT DUKES, M.D., F.R.C.P.

I. Introduction.—Efficiency for the accomplishment of the work of life is a result both of the character and direction of the training received, and of the physical and mental vigour to which that training has led. And, surveying the question from a practical point of view, it is obvious that greater "staying power" and less training is better than excessive training with consequent diminution of vigour.

Two-thirds of the period of youth are spent in the process of education, and in proportion to the care and thought expended by parents and teachers will growth and development reach their highest expression, or ill-health and disease result. I have no hesitation in saying, from a wide experience, that a due amount of care has never yet been bestowed upon the young human being. Yet, in his training the same scientific

methods which are employed in the rearing of domestic animals are essential.

In the training of the young the individual must be regarded as a whole, so that mind may not be developed at the expense of body, or *vice versâ*, but a harmonious dual development secured. In place of this rational course the teacher, at the present time, is too apt to endeavour to pass all his pupils through the same process, regardless of differences of individual character and capacity; with the result that the capabilities of many pupils remain dormant or stagnant, while others are forced beyond their powers.

In the process of education, which in its proper sense necessarily implies both physical and mental development, the teacher too frequently ignores the former factor. It is the physician's province to point out that education must not be pursued at the expense of physical welfare. Though his advice may be too generally ignored or contemned, he must yet insist that his office is to guide the schoolmaster in his duties so far as they concern the health of the pupils; nay, even in respect of the teaching itself—so disastrous is the assumption that teaching needs no technical training—less serious consequences would ensue to the young were the physician's advice more frequently sought and adopted.

The proper aim, therefore, of parents and teachers being the attainment of the highest development of mind and body, it must be impressed upon them in every way that this result is dependent upon an appropriate training in youth.

In order to secure the highest physical growth it is necessary that an approximately accurate estimate should be formed of each child's constitution. Those who should receive the most careful forethought are:—

1. Children who are delicate or sickly.

2. Children who have had an ailment which may recur in unfavourable circumstances.

3. Children who, though healthy as yet, come of an ailing or diseased stock, a stock in the offspring of which, as the physician knows, hereditary ailments and diseases are apt sooner or later to appear. If these children be surrounded by favourable conditions during the period of growth, the tendency to such disease might be eradicated or mitigated. Partly through ignorance, but mainly from pure thoughtlessness, parents flatter themselves that, as their children seem healthy during youth, they have escaped the parental tendency; whereas if they would but admit that these children are likely to be stamped with their own die, and set themselves diligently to counteract the hereditary taint, the children would often have to bless this wise forethought for a healthy manhood.

It is incumbent on parents to bear in mind what is so well expressed by Dr. John Harley, that "within certain limits the healthy body can accommodate itself with facility to considerable variations in the external conditions, and those are the delicate who cannot readily do this, and who, in the transition process, are liable to develop abnormal

action, or, in other words, disease." To ignore such tendencies to disease may hamper the child throughout life, and bring misery not only to himself, but possibly again also to his descendants, by entailing disease and premature death, or, still worse, that deterioration of character which ill-health so often engenders.

TABLE showing the average and mean height and weight, and the annual rate of increase, of 7855 boys and men, between the ages of 10 and 30, of the *artisan* class—town population :—

Age last Birthday.	Height, without Shoes.				Weight, including Clothes of 9 lbs.			
	Average.	Growth.	Mean.	Growth.	Average.	Growth.	Mean.	Growth.
	In.	In.	In.	In.	Lbs.	Lbs.	Lbs.	Lbs.
10	50·52	...	50·50	...	66·31	...	66·0	...
11	51·52	1·00	51·50	1·00	69·46	3·15	70·0	4·0
12	52·99	1·47	53·50	1·50	73·68	4·22	74·0	4·0
13	55·93	2·94	55·50	2·50	78·27	4·59	78·0	4·0
14	57·76	1·83	58·00	2·50	84·61	6·34	84·0	6·0
15	60·58	2·82	60·50	2·50	96·79	12·18	94·0	10·0
16	62·93	2·35	63·00	2·50	108·70	11·93	106·0	12·0
17	64·45	1·52	64·50	1·50	116·40	7·66	116·0	10·0
18	65·47	1·02	65·50	1·00	123·30	6·97	122·0	6·0
19	66·02	0·55	66·00	0·50	128·40	5·08	128·0	6·0
20	66·31	0·29	66·25	0·25	130·60	2·20	132·0	4·0
21	...	...	...	...	...	...	...	...
22	66·60	0·29	66·50	0·25	135·40	4·81	136·0	4·0
23–30	66·68	0·08	66·50	...	139·00	3·58	138·0	2·0

TABLE showing the average and mean height and weight, and the annual rate of increase, of 7709 boys and men, between the ages of 10 and 30 years, of the most favoured classes of the English population—public-school boys, naval and military cadets, medical and university students :—

Age last Birthday.	Height, without Shoes.				Weight, including Clothes of 9 lbs.			
	Average.	Growth.	Mean.	Growth.	Average.	Growth.	Mean.	Growth.
	In.	In.	In.	In.	Lbs.	Lbs.	Lbs.	Lbs.
10	53·40	...	53·00	...	67·4	...	67·0	...
11	54·91	1·51	54·50	1·50	72·9	5·50	73·0	6·0
12	56·97	2·06	56·50	2·00	80·3	7·39	80·0	7·0
13	58·79	1·82	58·50	2·00	88·6	8·27	88·0	8·0
14	61·11	2·32	61·00	2·50	99·2	10·61	98·0	10·0
15	63·47	2·36	63·50	2·50	110·4	11·21	110·0	12·0
16	66·40	2·93	66·50	3·00	128·3	17·92	126·0	16·0
17	67·84	1·46	68·00	1·50	141·0	12·69	140·0	14·0
18	68·29	0·43	68·50	0·50	146·0	4·97	146·0	6·0
19	68·72	0·43	68·75	0·25	148·3	2·20	148·0	2·0
20	69·13	0·41	69·00	0·25	152·0	3·87	150·0	2·0
21	69·16	0·03	...	...	152·3	0·27	152·0	2·0
22	68·93	...	...	...	154·7	2·44	...	...
23	68·53	...	...	...	151·7	...	...	...
24	68·95	...	...	...	149·2	...	...	...
25–30	69·06	..	69·00	...	155·2	0·42	154·0	2·0

The *height and weight* should annually increase, not, it is true, with steady regularity. For spring and early summer are the periods of maximum growth in height, and minimum growth in weight; while autumn is the period of maximum growth in weight, and of minimum increase in height. In winter the increase in height and weight are diminished; and in certain years the height increases more rapidly than in others. But the weight always bears a certain definite ratio to the height.

In a child a constitutional disease is usually regarded as a necessary evil, and the parent never dreams that a rational readjustment of the circumstances in the light of modern preventive medicine might have obviated the mischief.

We should never forget that a vigorous manhood is the greatest of all blessings, and that the vestibule to its attainment is a healthy childhood; parents must be educated to understand that the highest and most acceptable endowment which they can bestow upon their children is good health, and *after* that, a sound education; by forethought and foresight these blessings may usually be obtained.

Health must depend largely upon two conditions:—

1. The inherent properties of each individual.
2. The environment in which the individual is reared.

Only so long as the individual organism is placed in its appropriate surroundings—*i.e.* grown on its proper soil—can we expect to produce typical health and strength. Failing these necessary conditions we can only anticipate imperfect growth, meagre health, an absence of robustness of character and manliness, the manifestation of early disease, and the absence of vigorous old age.

II. The Environment.—I would first point out the necessity, as far as possible, of bringing up the young in the country rather than in town; and in detached residences, rather than in the immense blocks which constitute some of our schools and asylums. Where parents reside in towns every effort should be made to arrange for education in the country; if this be impracticable, opportunity should be made for spending the vacations there. The importance of this condition has repeatedly impressed itself upon my notice, when I have been consulted about the children of persons in comfortable or even in affluent circumstances who (with apparent exemption from any hereditary delicacy in the family) enjoyed all the requisites for healthy growth except this: and who, being brought up in a town, or even in a "healthy suburb," continually suffered from tonsillitis, croup, bronchitis, persistent bronchial catarrh, or pneumonia. As soon as they were removed to a school in the country their ailments ceased, education was uninterrupted, and healthy physical development succeeded. In the case of nervous diseases this difference of effect between town and country is still more marked.

When I joined in the inspection of a Volunteer brigade of five battalions comprising more than 4000 men, I observed in passing

through the ranks of the various "companies" that the difference in height, breadth, and aspect between companies levied in the country and those mustered from towns was astounding. These facts are clearly exhibited in detail in the carefully prepared tables of the late Mr. Charles Roberts, which should exercise a decided influence on the modes of rearing the young.

The air of town and country is, of course, originally the same in composition. But town air is rendered impure, not only by the absence of sunlight, but, as it would seem, by the presence of some deleterious elements. Hence the exhilarating feeling of breathing fresh country air as a contrast to that of the town. But the utility of transferring children to the country vanishes if they are confined to day-rooms and bedrooms with such insufficient *cubic space* and ventilation that air has to be rebreathed.

There is no habit more common, and none more deleterious and uncleanly, than that of living, working, and sleeping in ill-ventilated rooms, and breathing and rebreathing the same air. It causes ill-health and deficient growth, from the imperfect working of the internal functions of the body; and renders the human being disposed to the attack of poisons from without. There can now be little doubt that these conditions pre-eminently favour the development of tubercle bacilli. The effect of pure and impure air on health and mortality, as recorded by Parkes, is strikingly shown in horses; for in them the question is more simple on account of the similarity in different times and places of food, water, exercise, and treatment. Formerly, in the French army, the mortality of horses was enormous. Rossignol states that, previous to 1836, the mortality of the French cavalry horses varied from 180 to 197 per 1000 per annum. The enlargement of the stables—the increased quantity of the ration of air—reduced the loss in the next ten years to 68 per 1000.

It is sometimes stated that nurseries and schools need only be supplied with half the usual air-space, on account of the size of the inmates. No greater mistake can be made. Children cannot thrive well without the purest air; like the young of all animals, they are peculiarly sensitive to pre-breathed air. Yet parents will take any trouble, and make any complaint, about the quality and the quantity of the food at schools, but show no concern about the ration of air provided. If they have to find fault with the appearance of their children on their return home for the vacation, they immediately throw the blame on the inferior quality or quantity of food. The truth is that, in a large proportion of cases, the pupils are compelled to live and work hard in insufficient air-space, and to sleep in still less. This has been repeatedly proved by the diminution of excessive mortality on the provision of more air. The active functions of children, together with their quicker breathing, necessarily produce more rapid tissue change. It was found by Voit, that during waking hours more carbonic acid in proportion is given off, while during sleep more oxygen is absorbed than carbonic

acid eliminated. And in his eighth report to the Privy Council, 1865, Sir John Simon stated, "that even healthy children, in proportion to their respective bodily weights, are about twice as powerful as adults in deteriorating the air which they breathe."

Place.—The surface of the soil is usually loam, and is much the same in all situations. It is loaded with decaying animal and vegetable matter, which, in favourable circumstances, is kept sweet by the aid of bacteria. If this decaying organic matter be in greater quantity than the bacteria can destroy, as in made ground, the *ground air,* saturated with carbonic acid, and other gases evolved during decomposition, may very injuriously affect the inmates of habitations constructed upon the spot. The quality of the soil on which the child is reared is of paramount importance, especially in relation to the amount of this organic matter, and the position of the *water-level.* It is well known that water lying stagnant on the surface of land is very inimical to health; but it is not so well recognised that unhealthiness is also produced where the subsoil is *water-logged, i.e.* loaded with stagnant water.

Drainage of Soil.—Efficient surface and subsoil drainage, so as to lower the water-level even a foot or two, may banish pulmonary tuberculosis and diarrhœa from an entire district, and produce so improved a state of health among the inhabitants that the development of germ life in them is largely prevented.

In the selection of residence for a *delicate child*, other things being equal, the nearer it is to the sea the more equable the climate; the farther from the sea the more is the climate one of extremes. Hence the child who requires a moist, equable climate, with warm winters and warm nights, should live at the sea-side, while those who need a more bracing air should reside inland. Children who possess that form of delicacy which renders them susceptible to *constant colds*; those having a hereditary tendency to *rheumatism*, *consumption*, *feeble circulation*, *neuralgia*, *kidney disease*, and other such misfortunes, might be saved much misery could they pass their period of youth in a dry, warm situation. It must constantly be borne in mind, that although consumption is a parasitic disease arising from the attack of tubercle bacilli, yet these bacilli only find a suitable soil for their propagation in certain constitutions, or in feeble states of constitution; a vigorous condition of health resists them.

Further, where insanity, or even an excitable nervous condition—which is often exemplified in hysteria only—is known to have occurred in members of the family, the child should be educated where he can be out of doors most of his time on fine days, so that vigour of constitution may be produced, for in this development the brain itself largely participates. Such a child should not be allowed to work at night, or for any examination, until his brain is mature in its growth. Above all he should be taught that immorality in any form is especially detrimental to the stability of his brain.

It is also imperative that a child born with this hereditary dis-

position should be educated, from his earliest years to manhood, away from home, and apart from the management of his parents or any relatives who are tainted with the nervous constitution, in a place where a regular life will be maintained under watchful discipline, where all waywardness will be dealt with by a firm but kind hand, and where he will work and play with those of his own age who are more robust in health and in character. By such means the nervous tendency may be eradicated; yet these very children are too often kept at home, where they are petted and pampered, never thwarted or corrected lest the nervous condition should be induced, and where peevishness, ill-temper, and petty tyranny are allowed full sway. Such surroundings make a hotbed for the development of the tendencies which it is essential to check. In the case of girls, who spend so much time at home, and are disposed to a nervous habit, it is still more imperative that their education should be absolutely freed from the influence of such surroundings.

It is most mischievous to tamper with the *emotions* of the young, for they are so unstable during this period of life as to be certain to run into channels unforeseen and undesired. Even religious fervour, if excessive, is often perverted into the shape of sexual immorality. In youth the appetites, desires, and passions awake, untempered by reason, uninstructed by experience, so that at no time of life is steadfast guidance and help more essential. Yet how few boys—and still fewer girls—receive the needful aid from their home training; a *policy of silence* is substituted with results frequently disastrous.

III. External Conditions.—As regards *clothing*, it must be borne in mind that the skin is our most important gland, and requires protection to enable it to do its duty, and to prevent its functions being arrested by sudden chills or other changes of temperature. In this country, where the temperature of the body is always higher than that of the atmosphere, the use of clothing is to prevent the waste of the heat of the body.

The skin regulates the temperature of the body by means of its blood-vessels, and these are dilated and contracted by their vasomotor nerves, which turn on or shut off the blood as stopcocks regulate hot-water pipes. The equability of the temperature of the body is regulated by a mechanism now well known to physiologists. The cooling power of a sweating skin is enormous, and the chill arising from clothes damp after exertion or getting wet is well known. But no one catches cold, or becomes chilled, from keeping on wet garments so long as he is warmly clad, *i.e.* so long as rapid evaporation or icing is prevented. A non-conductor should, therefore, be worn next to the skin, in order that the changes of its temperature may not be too sudden. Wool of various thickness is the best covering of the skin in summer as well as in winter. It should be remembered that the bodies of children are less capable of resisting heat and cold than of adults. But the worst of all clothing for children is *excessive* clothing. From time to time I see children who,

being considered delicate, are burdened with an inordinate amount of clothing which increases their delicacy—their skin is never dry. By a reduction of the excessive clothing the "delicacy" usually disappears. Clothing should keep the skin warm, but not moist except under active exertion. When moisture is perceptible on the skin in ordinary circumstances by night or day, the clothing is excessive and harm will result. In this country the summer season should be well established before a change is made in the thickness of the underclothing; much illness is occasioned by a premature change suggested by a few warm days in April or May.

Much care should be given to keep the *feet* always warm, for neglect of this entails unnecessary ill-health often wrongly attributed to inherent delicacy. I continually see children, and whole families too, who are always ailing, and are consequently described as very delicate; whose "delicacy" comes indeed of the mother, but only in this, that she does not know the value of warm dry socks and thick boots. That the lack of these is the commonest cause of enlargement of the tonsils I feel sure, and I suspect that it is answerable for a large proportion of the cases of post-nasal growths.

The importance of warm feet in the maintenance of good health has so impressed itself upon the attention of a shrewd schoolmaster who has 125 boys under his care, that every boy is compelled daily, as soon as he has settled indoors, not only to change his boots, but also to put on a pair of dry socks. The *drying of damp boots* before rewearing them has not yet received the attention it deserves, and in very few schools are means provided for this purpose. The miseries and deformities (such as chilblains, ingrowing toe-nail, flat foot, anchylosed toes, and corns) originating from out-grown and misfitting boots—boots never intended to fit the foot, but only to suit the fashion—I must not here discuss.

IV. Internal Conditions.—Next in importance to fresh air, sunshine, and locality in the nurture of the young is the material—*food*—necessary to provide for existence and for growth and development. Without nourishment, appropriate in quantity and quality, bodily vigour is impossible, resistance to parasitic disease fails, internal maladies arise, or less specific general physical and mental deterioration are induced.

The primary fact in the feeding of the young is, that the food consumed has not only to nourish the existing tissues, but to provide for their further growth. Abundance of food is therefore necessary. The amount which children can eat, though astounding, can safely be allowed, provided it be plain, wholesome, and appropriate for the nourishment of the tissues. Yet adults perpetually assert, with wonder, that children eat more than they do themselves. Naturally they do, or ought to do; and if they fail to do so, the prospect of vigorous growth is seriously impaired. For in children, compared with adults, much more constructive work has to be accomplished by food; and, indeed, so imperative is Nature's demand for food at this stage of physical development, that

growth of a kind will even be effected at the expense of the repair of tissue. So urgent is the demand for food in the young that, when starvation arises, as is sometimes seen on the ocean in case of shipwreck, the younger are the first to succumb. The experience, again, in famines in India has too often shown that a bare subsistence-diet without work, especially in the young, becomes a starvation-diet when work is added; and this observation applies equally to mental and physical work.

While it is only too easy to overfeed the adult, superabundant nourishment is almost impossible in those still growing, provided the food is not rich in quality,—the latter element more rapidly producing physical disturbance in the young than in the adult. Those who genuinely attend to the welfare of children should accept as an axiom that a healthy child's appetite is the surest guide to the requisite amount of food, so long as it is plain and wholesome. Children may, however, be readily surfeited by too many delicacies.

A large proportion of the sufferings of adult life arise from the inappropriate food and cooking and the hasty meals of adolescence. Sometimes the diet of youth is so nicely adjusted to its cost that illness is barely averted, while growth and development are frustrated. A more short-sighted policy, even financially, it is difficult to conceive; the cheapest policy in the long run, for the rearing of youths, is to feed them well, so that they may be advantageously started for the attainment of the maximum of size and strength. If thus helped to reach a vigorous adult age, greater and better work will be obtained from them, with more vigorous brain-power, higher character, and less liability to special incapacities or deficient energies.

Again, *variety of food* is essential to efficient digestion and liveliness of disposition; monotony of diet seems to produce monotony of character, probably by way of some defect of nutrition.

The periodical use of the scales—say once a month—would indicate to parents and teachers beyond all doubt whether the child was well cared for or gravely wronged. It would reveal errors in the mode of life,—such as inappropriate, insufficient, or monotonous feeding, overwork, or over-exercise,—and would also direct earlier attention to the advent of disease. Periodically carried out it would show whether the natural standard of height to weight was being maintained.

In estimating the significance of the measure and scales, it must be remembered that most children grow by fits and starts; rapid growth requires great care, ample food, more rest, and little work, while on loss of weight work should be diminished or cease altogether. In some schools such a record is already kept, and has been found to be of the greatest assistance to the teacher. For instance, should the measure and scales disclose that all the pupils are deficient in height and weight for their age, it will be evident that some radical defect of management exists; should they indicate that one child here and there is below the average, a reference to the height and weight chart on entrance to school might show the child to be the offspring of a diminutive stock:

on the other hand, if the original height and weight were then normal, the evidence would be clear that the child had been working excessively, fed too sparingly (perhaps on account of a squeamish stomach), or that illness or disease was imminent.

On the other hand, it is quite conceivable that many schoolmasters and mistresses would dread the introduction of this system, since it would reveal the viciousness of many of the present methods of education and treatment, and would involve (if its indications were attended to) considerable thought and alteration in the administration.

No work should ever be imposed upon boys or girls without previous sustenance. Food first, work afterwards, should be the invariable maxim. To work before food probably implies that the material necessary for the performance of the work must be absorbed at the expense of the system and to the hindrance of bodily growth. The meals, therefore, should be wisely arranged: a substantial meat meal should be provided for breakfast and dinner, so that the heavy meals may be consumed before the principal morning and afternoon work commences; lighter meals may be taken in the after-part of the day, when the heavy work is ended. On the other hand, a meat meal three times a day is objectionable and injudicious on all grounds; although I continually hear of physicians recommending this plan in the rearing of youth, it would be found most inappropriate for schools at all events.

The *cooking* of food for the young has scarcely received the attention it deserves and requires; this neglect and the supplementary stuffings at tuck shops are a fertile source of feeble health, meagre work, bad temper, and permanent damage to the digestive organs.

Sufficient *time*, again, is rarely allowed to the young for efficient mastication and saturation of the food with the secretion of the salivary glands. If a child abstain, for any reason, from eating a meal or meals, he must not be expected to perform his tasks as usual. Every child who does not eat his food should be known, careful inquiry made into the cause, and the omission repaired. It must never be forgotten that it is during the years of growth that the delicate child may overcome its feebleness and be made permanently strong, or the strong child be weakened and stunted. In feeding the young, *short intervals between the meals* are necessary in consequence of their quicker digestion and their naturally greater demand for food.

I would especially point out the necessity of children being taught to use their *teeth* for the purposes of mastication; in this way only will the teeth be kept serviceable. For there can be no doubt that the main cause of the deterioration of the teeth in civilised races arises from their insufficient use owing to the employment of the knife and fork in their stead, and the artificial preparation of the food consumed. A cogent reason signifying the truth of this is the gradual shortening of the jaws, and the stunted character of the wisdom teeth in civilised races. Twice a year at least children's mouths should be inspected by the dentist.

Concerning the suitable *kinds of food* for youth, I would insist that

meat should be provided twice a day, at breakfast and at dinner; that *vegetables* and fruit are important elements in the diet of youth; that the crust of *bread* is more suitable than the crumb, and whole meal than white bread; that *porridge* is an invaluable article of diet; that *sugar*, so frequently denied, is an indispensable requirement, forming as it does their main heat-forming food, as well as the most important factor in the growth and work of muscles; that *milk* should take the place of tea and coffee; and that young people are better without *alcohol* during this period of life.

Food implies *waste*, which results from wear and tear, and is removed from the body by certain excretory organs. These products of combustion must be continually removed if health is to be maintained. As Sir Lauder Brunton says: "As a rule, people are now fully alive to the risks they run from poisoning by sewer gas, or to put it more widely, from poisoning by products of decomposition *outside* the body; but perhaps we do not all of us keep so clearly before us as we ought the fact that *inside* the body there are all the conditions for the formation of putrefactive products, and the most favourable arrangement for their rapid absorption." The need of the daily removal of these products from the body is not yet sufficiently taught and enforced in the young, and as a consequence much unnecessary ill-health ensues, and the appearance of piles is facilitated and encouraged.

V. The Education of the Intellect.—As we have discussed the suitable environment for the human body during early life and also the material necessary for growth, we must now consider the purport of this care, and we shall find that the highest attainable development is impossible without the *exercise* of functions.

As unused organs atrophy, it is, therefore, essential that they be employed in order to ensure a maximum of growth and usefulness. But it must be borne in mind that whether we consider the exercise of the brain, which during this period of life we shall term *work* or *education*, or the exercise of the body, which we shall term *play* or *recreation*; exercise increases growth, while over-exercise stunts it. This is doubly true when we are discussing immature but growing organs; for strain of any description is detrimental to their efficiency. And exercise of function is not only essential to growth and development, but also to the healthy maintenance of the brain and body when normal growth is attained. In the performance of work, energy is expended and finally exhausted; and this end comes sooner in the young—owing to deficient "staying" power—than in those whose tissues are matured. Moreover, the young have to tread unbeaten tracks, which consumes more force than the pursuit of more or less accustomed studies. This opening up of new ground necessitates exertion, and unless the exertion is put forth with pleasure, it is apt to become harmful; whereas information acquired by the young with pleasure rarely occasions injury. Hence the importance of the study of "likes and dislikes," and of fostering work for which the pupil shows a taste, slowly adding that which is at first dis-

tasteful. In fact, the appetite for work is very similar to the appetite of eating; the child will not only thrive, but get fat on that which it likes, while it will eat so sparingly of what is distasteful that the body will suffer. It is true of mind as well as of body that we all, if unsophisticated, like what we can readily digest. Moreover, as variety of food is essential for the adequate development of the body, so variety of work is imperative for due development and nourishment of the brain; and as slow and regular development of the body produces the finest and most permanent results in strength and durability of other tissues, so it is also with the brain itself.

The prime duty of the teacher is to develop whatsoever faculties a pupil has, however rudimentary they may be; and he alone is the real educator who knows how to compass this, instead of passing all pupils, like corn, through the same mill. Every faculty thus developed becomes a stepping-stone in educating other faculties which may be still dormant; though sometimes special ability in one direction may coexist with utter incapacity in others, mentally and morally. It is natural to all children to desire knowledge,—a desire which, unfortunately, our teachers too often succeed in extinguishing outright.

The true aim of training and of education should be to develop the best type of manhood in mental, moral, and physical well-being,—an aim, I regret to say, too frequently disregarded, especially in the training of girls, who should receive the greater consideration on account of the peculiarity of their growth and the demands to be made upon them in early motherhood. The young are allowed insufficient time for sleep; they are often deprived of fresh air and exercise by faulty school regulations, or unwisely assigned punishments; they have little time to masticate their food owing to the hurry of school customs; and their hours of work are usually too prolonged, extending throughout the evening and too far into the night, to permit either of good work or a healthy development of the brain. An intimate friend, and a born educator of the young, has informed me that since he abolished evening preparation of work in his school of considerably over a hundred young boys, not one case of sleep-walking has occurred, although many cases happened before this reform.

The worst feature in this prevalent method of education is that the long hours and clumsy educational methods compel the work to be performed under a sense of fatigue, so that the work itself is not of lasting value, and the brain may be damaged in the process. These imperfect methods of education are likely to continue until teachers receive a technical training in their duties, or at any rate till they cease to despise and abhor it. The education of the youth of the upper and middle classes in England is the only business for which a man is not trained.

The successful educator considers his pupil as a whole; it is the disregard of this unity that leads to harmful results. Each child possesses but its own proportionate stamina and mental ability, inherited and acquired. The ability may exist potentially in abundance, but of

what avail unless the stamina be sufficient to provide a plentiful supply of good red blood for the sustenance of the brain? This brain nourishment is the product of an efficient digestion of food, appropriate in quantity and quality, of *fresh air* and *exercise*, and of ample *sleep*, for the nutrition of the brain takes place mainly during sleep.

It is one of the most obvious physical laws of nature, holding good throughout the entire animal creation, that immature organs are incapacitated and deteriorated by excessive work; while they are developed and rendered vigorous and active for adult life by sufficient healthy and graduated exercise. But the exercise should be progressive, not stationary; for mental and physical exercise fit for a child is not sufficient for a boy, and exercise suitable for a boy is not adequate for a man. The converse is also true: that the exercise adapted to a man is too severe for a boy, and what is suitable for a boy is abnormal for a child.

In the regulation of the *hours of work* will any sane man uphold the invariable custom which prevails of assigning the same number of hours of work to a young child when he enters school and to a senior pupil at the point of leaving? It would be as reasonable to expect him to undertake work of a similar order of difficulty. To some extent it is recognised that one of the chief functions of the competent educator is to graduate the training of the brain from short and easy tasks to more rigorous and strenuous exercise; but the length of the hours of work should be similarly gauged, as the young are without that power of sustained endurance which comes only with the completion of education. Moreover, it is an established fact that the best work is not obtained at schools where the hours are longest and the pressure most severe. If sterling and lasting work is to be accomplished during youth, and the brain is to be benefited in the process, teachers must learn that the work of the immature brain must be proportioned in difficulty and duration to its age and capacity. Yet the work assigned is sometimes so disproportionately severe that progress is arrested, or too often converted into retrogression; at other times the work is too prolonged, and tells its tale in weakened brain, body, and interest; the character also suffers, in consequence of the temptation to employ illegitimate means for its accomplishment, or to avoid punishment on account of failure. A *scale of work* should be adapted to each age; and this again will require revision and remission in certain cases and in special circumstances of age and sex. In this scale should also be included any work assigned as punishment.

Table of the Scale of Work.

Ages	Hours of work per week.
From 5 to 6	6
„ 6 „ 7	9
„ 7 „ 8	12
„ 8 „ 10	15
„ 10 „ 12	20

Ages.	Hours of work per week.
From 12 to 14	25
„ 14 „ 15	30
„ 15 „ 16	35
„ 16 „ 17	40
„ 17 „ 18	45
„ 18 „ 19	50

Each faculty of the brain—such as thought, memory, special sense, muscular co-ordination, and other functions—requires its own special stimulation for purposes of development. Every brain has its natural high-water mark of effort and capacity. The systemic circulation of the blood affects the central circulation so intimately that on it depend not only the growth of the brain itself, but its functions also during the process—a full circulation aiding a flow of ideas and the retention of facts. The debility of more rapid growth—occasionally seen in boys, and habitually in girls—like that ensuing on illness, causes a feebleness of circulation, and in consequence apathy and incapacity for mental exertion, however eager the pupil may previously have been in the acquisition of knowledge.

An inferior *quality of the blood*, like a feeble circulation, dulls the mental faculties, as in anæmia, whether arising from deficient food, loss of blood, or overwork. No less injurious are the *impurities* which may circulate in the blood, and so irritate the brain matter as to give rise to all the symptoms of overwork, as is seen in the case of constipation, biliousness, albuminuria and so forth. It is therefore manifest that brain capacity, although in part it depends upon progenitors, depends also in part on environment. The bounds of safety can easily be overstepped where graduation of the amount and difficulty of work is not provided for.

It is not always the bright and promising pupil, but frequently the dull, feeble, though conscientious one who is overpressed. Moreover, there are grades of overwork, from poor health and loss of weight to a complete and often permanent breakdown; here it is that the scales tell so genuine a tale. Loss of weight—and even a stationary weight—during the years of growth means overwork, underfeeding, incipient disease, or recent illness. Yet children, while suffering from illnesses or well-marked functional disturbances, are often kept fully at work as if in robust health. The converse case is only too common, in which a brilliant pupil from too early pressure becomes a nonentity, with an impoverished and incompetent brain.

It is consequently incumbent on those who have the welfare of the young at heart to gauge the material with which they have to deal; and we repeat that it is essential for teachers to be adequately equipped with the requisite judgment, the necessary technical skill in teaching, the tact and force of disciplinarians, and a knowledge of the physiological factors concerned. The circulation of blood in the young brain is always in excess of that which exists when maturity has been attained, and thus

provision is made for the more rapid repair and growth. Moreover, all mental work makes the blood-vessels distended and the brain hyperæmic. If during this period of life work be too prolonged, and this pressure too frequently repeated, the blood-vessels do not recover during the brief periods of rest. In this way the brain becomes congested, and œdema of the cerebral tissue follows with alteration of function, symptoms of headache, sluggishness and perversion of thought, absence of mind, irritability, inability to fix the attention, which may lead even to organic diseases of the brain of various kinds.

The teacher should, therefore, have an adequate acquaintance with physiology in its relation to the structure and functions of the brain. Even tillers of the ground are now taught the properties of the various soils they have to till, and their relative suitability for special crops. The knowledge of the relation between mental capacity and head diameters is of fundamental importance: the relation between the transverse diameter and the capacity is more significant; and the more the cranial cavity's contents are increased, the greater is its tendency to assume a spherical shape.

In a large proportion of instances an early "scholarship" is positively harmful to the individual child. In the working for scholarships some of the competitors have to concentrate their whole intellectual energy, day by day, for many consecutive months, and in the end suffer from mental exhaustion; while others will not require to exercise one-fifth of their mental power to accomplish exactly the same task. In the former case, while the scholarship may be attained, the competitor is damaged for life in the attempt: in the latter he emerges unscathed. How is it known when undue strain is occurring? When the usual rest fails to efface all the effects of the work and restore complete renovation.

It behoves the physician of the present day, however, to be exceedingly cautious in suggesting to schoolmasters that a certain brain is incapable of bearing the strain imposed, for the demand for our public schools being greater than the supply, the unfortunate pupil who may only require, in order to enable him to compass his duties, a little consideration in easing or lessening his hours of work and increasing his sleep, may not receive the required sympathy, but may be told that if he cannot keep in the running his place must be filled by another eager applicant; his future career may thus be compromised. The brain wastes in all illness, and this atrophy renders it totally unfit for work, or even for reading a difficult book for a considerable time. I have not yet succeeded in impressing upon parents and teachers that, so far as one can judge from the apathy exhibited in these cases, and the easily induced fatigue, as well as from observation of nature, the brain wastes in equal proportion to the waste of the body.

It must also be remembered that knocks on the head, to which boys are liable from various causes, may alter the nervous structure, possibly from bruising and minute ruptures, and that prolonged cessation from

work should be enforced even when the blow may have been of a comparatively trivial nature. [*Vide* art. on "Concussion of the Brain."]

But overwork is yet more pernicious in its effects when the necessity of an ample allowance of *sleep* is not recognised. It is a well-established fact that more sleep is required for the formative than for the intellectual activity of the cerebral centres; yet what a record do our schools furnish in this respect! It must not be supposed that the deleterious effects of overwork during youth can be compensated by an additional amount of sleep, for nature will not permit a forced brain to rest—one of the most manifest symptoms of undue pressure being wakefulness. The over-exercise of the animal functions nature does not resent, for the more the muscles are used the more the brain will rest. Teachers should know that deficient sleep means stunted brain and body, and must not forget that it is only by graduated exercise of the mental faculties that the highest condition of brain development may be secured for work in after years. Yet the child on entering school is only allowed the same number of hours of sleep as the big boy who is leaving, whereas two hours more should be allotted, as the following table shows:—

THE AMOUNT OF SLEEP REQUIRED DURING YOUTH.

Age.	Hours of Sleep.
Under 10 years	11
„ 13 „	10½
„ 15 „	10
„ 17 „	9½
„ 19 „	9

But while the child's brain may be perfectly satisfied on this scale until the advent of puberty, yet for some time before and after that date, perhaps a year—when the growth is enormous, especially in the case of girls, and the development of new organs entails a severer stress upon the system—this amount is insufficient, as much more sleep is required for growth than for repair.

VI. The Exercise of the Body is necessary to attain a Maximum of Growth and Vigour.—But the brain can never attain its largest growth nor its highest quality of nervous tissue from the exercise simply of its own functions, for it is dependent to a large extent upon the vigour of the body, which is the manufacturer of the material on which it lives. As I have already pointed out, the growth of the brain depends upon the condition of its blood-supply; and the condition of the blood is dependent upon the state of the circulation, respiration, and the muscular and digestive systems. Hence the importance to the young of sufficient exercise. This exercise should take the form of games or recreation, in which refreshment the brain participates, rather than the form of a set lesson in the hands of a gymnasium instructor or the drill sergeant. These latter modes of exercise are desirable enough,

but they should be an addition to, rather than a substitute for *school games.*

Exercise during youth is excellent: games are invaluable. We, as a nation, owe our success chiefly to our mental and bodily vigour,—a vigour which is irrepressible, and dependent mainly upon the games of boyhood, which render possible our sports of manhood. What other nation would dream of playing football in India and polo in Burmah? The physical education of the young trains them in perception and judgment, as well as in adroitness and courage. Even yet, however, the influence of physical education on mental and moral growth is not sufficiently regarded, nor is it yet fully recognised that bodily and mental culture must be concurrent if the highest development is to be attained. The sportsman precedes the missionary; the missionary, the trader, in new countries; and the trader the statesman. Think of the joy of proficiency, the delight engendered by knowledge; and how, when a game is played, malice and ill-temper just filter away unobserved. What a training for life! These qualities can be developed in our school playing-fields; let them, therefore, be encouraged in every possible way. No question in the training of the young is of more general importance than the mode of occupying out-of-school hours. This freedom from work should be a period of cheerful recreation and constant lively occupation, otherwise it becomes a time of weariness and idle lounging, and the character and tone of the young must consequently deteriorate.

In physical exercise all the functions of the body are engaged; the circulation of the blood is quickened, more oxygen is inhaled, and the impurities of the blood are thereby oxygenated and destroyed, so that the excretory organs of the body may remove the detritus from the system. Observe the young boy who is keen in games, and compare his physical condition with that of the dawdler. Notice his healthy complexion, good wind, elastic gait, splendid muscles, increased stature, and sure promise of vigorous manhood. Consider, again, how boys' games tend to develop a well-balanced mind and character; how they instil, as nothing else can, glowing spirits from the robustness of health, quick response to calls of duty, frankness of disposition, good temper often in trying circumstances, love of justice and fair-play, self-reliance, endurance, confidence in comrades, desire to excel, quick judgment, aptness to act with others for the good of all, courage under pain or difficulties, self-control, and last, but not least, how they check morbid desires and sensations by the expenditure of superfluous energy, which ensures purity of life. In fact, most games provide exercise to muscles and brains, and involve both rapidity of observation and quickness of decision. In this way they are educated in a habit which will help to make them excel in the battle of life. How many men have learnt in their school games, in spite of many failings, to "play the game" of life with fairness. The future is almost hopeless for a boy who at school practised dishonesty in his sports.

Further, it was the development of games which abolished boys' fights at school. And if school games had no other salutary influence

than that of affording a wholesome topic of conversation in out-of-school hours, they would be worth the infinite trouble which should be bestowed upon them.

In the regulation of the games of the young, where healthy rivalry may, in the inexperienced, lead to excessive competition, I think the physician should have a voice. I would therefore suggest the following precautions, which are reasonable, without the unnecessary fuss which pupil and teacher alike resent :—

1. The physical examination of all children when they first enter school. In this way only can the healthy be safely compelled to play all games.

2. The proper apportionment of exercise consequent on this examination, in order that the physically weak, diseased, or deformed may be restricted to that exercise which is suitable to each. In this way only should any boy be excused from the ordinary school games.

3. The medical control of all severe exercise, so that even those who are physically fit to undergo it may not be permitted to do so without prior and suitable training for the prolonged exertion. It is excessive exercise, or exercise imprudently taken, which is so deleterious to those who are growing; exercise in proper measure promotes health and strength.

Exercise should be gradual in its increase, or harmful results may follow. Those who think that because they have excelled at some exercise during one season they can resume it in the next season without fresh training, are likely to overstrain and injure themselves. If we do not, therefore, wish to hear of the dangers of rowing, of running, and of football, of the golf arm and of the tennis leg, the muscles necessary to these exercises must be trained by degrees at the commencement of each season. All muscles may be educated to any strain within reason, but unused muscles are unable to bear sudden or prolonged efforts.

Syncope in boys during exertion is usually attributed to exhaustion, but my experience has shown that, while it may in some cases be occasioned by the physiological condition of the heart and vascular system at puberty, or be due to a temporary dilatation of the heart resulting from active physical exertion in an unfit state of body, it is more frequently toxæmic, the excreting organs being inadequate to the new and sudden call upon them.

Physical education requires as much forethought, method, and application as mental, whereas too much routine is involved in both.

For all games entailing exertion the player should be clothed in flannel, which should be changed immediately afterwards and dried; where this care is not observed, chills and even dangerous illnesses are apt to arise.

It is customary for the young to undergo *training* for boating and other athletic sports. The purpose of training is to place the body in such a condition as to enable it to perform the hardest physical work rapidly, or for a prolonged period; it is, in fact, to produce the highest

possible state of health for hard physical work. The essence of training is that the heart and lungs should become accustomed to sustained exertion, and this should only be effected by degrees.

In training to obtain a good "wind," it is of the highest importance to avoid indigestion, for nothing more thoroughly defeats that end. Food, therefore, as I have said, should be eaten slowly and masticated thoroughly, and no food should be taken between meals. There is a fallacious opinion among all trainers, be they trainers of mankind or of horses, that to those under training the smallest quantity of fluid should be allowed; hence these persons often suffer from actual thirst. Many people do indeed drink more than is requisite to satisfy thirst, man being the only animal which resorts to this mischievous practice. It should be a rule with every one, in order that the highest condition of health may be attained, to take only a sufficiency of fluid, say from two to three pints daily, except in hot weather or under great exertion and sweating. Water sufficient to satisfy thirst should be freely allowed, but in small quantities at a time; thus the athlete never becomes actually thirsty,—for every ounce of fluid which leaves his body another is supplied in its place. Dry tissues and unnaturally thickened thirsty blood are unfit for the highest functional activity. To suffer thirst for minutes or hours, and then, when the exercise is over, to take, as many do, an excessive quantity of fluid, may well cause discomfort, take away appetite, and entail indigestion and loss of sleep.

Again, change of work and change of play are as important as variety in diet. At the present time the games of the young are too monotonous, and insufficient attention is paid to natural tastes and aversions. This is not the place to discuss the merits of the several games suitable for boys and girls during their growth; but I would point out that the exercise adapted to boys is also compatible with the health and physique of girls up to the age of puberty; after that age the games of girls should gradually pass year by year into exercise of a quieter character.

The exercise obtainable from games, as well as that from hand-culture, should be various, not only for the better development of bones and muscle, but also for the development of the brain itself, as every complex movement has its brain-centre, which, in its turn, is developed by the exercise of its functions; so that we want not only football, cricket, rowing and running, but, in addition, walking, brook-jumping, high-jumping, skipping, swimming, skating, racquets, fives, lawn-tennis, lacrosse, golf, hockey, baseball, wrestling, fencing, boxing, gymnastics, physical drill, cycling, rifle-corps drill, rifle-shooting, camping-out, workshops, natural history excursions, gardening, music, and drawing. With such variety of exercise, and mountaineering, riding, shooting, and fishing in the holidays, the brain and body will be formed as a complete and harmonious whole.

The physical education of girls is seriously neglected, and insufficient attention is paid to their bodily development. Why do girls so frequently fail in health directly they undergo hard mental work, sometimes becoming

incapacitated for life, physical wrecks, and the victims of hysteria and other neuroses? Simply because they and their friends attempt the impossible. If we are to have the higher mental education in girls, of which they are quite capable without injury, they must not be pressed, as they are at present, during those years when their growth and development are enormous, namely, from 11 to 14, when they leap, as it were, from childhood to womanhood at a bound, for all their nervous force is expended in this direction. Teachers must not fail to recognise the difference in constitution between the boy and girl. Continual application to work from day to day, from week to week, and from month to month, should never be required of girls; nor should they even be allowed to make such efforts; cessation and rest at menstrual periods should not only be encouraged, but even enforced. Their mental education, again, must proceed *pari passu* with a thorough physical education, otherwise, with rare exceptions, it must end in failure, perhaps in serious or life-long misery. If in Great Britain we cannot yet manage both, let the mental education remain as it was, and the physical education be undertaken more completely, so that girls may by degrees be prepared for the higher intellectual education, and become better suited for their womanhood.

At the present time a girl's education is *effeminate*, whereas it should be *feminine*. Why was it so long considered unladylike for girls at school to follow any other outdoor exercise than a formal walk in the street? There was no conceivable reason for this restriction. Many head mistresses have had the courage to break through the spell and establish good schools for girls, in which their physical education is as well organised as their intellectual and moral education. They deserve well of their country, and are carrying out one of the greatest and most-needed reforms of the age.

Girls are naturally more subject than boys to nervous excitement, but this is effectually restrained by a sound physical development. They are so often what they are—"nothing but nerves," or "nothing but emotions," ready to faint on any, or without any, provocation—because they suffer from faulty training and conditions unnatural to them; these evils will gradually disappear as girls are reared under a more reasonable system.

The absence of daily, regular, and sufficient exercise renders girls listless and apathetic, entails pallor and anæmia, constipation with its sallowness, foul breath, and depressed spirits, crooked and stooping backs, and knock-knee and flat-foot with characteristically awkward gaits.

It should be the aim of parents and teachers to instil into girls' minds the fact that it is their duty to try to be physically strong, and to provide for its attainment by adequate means. They should be taught the necessity of being vigorous as well as graceful, and naturally instead of artificially shapely. But this perfection of body can only be reached during the period of youth, and by physical exercise, which, duly regulated, promotes not only muscular development, but also a vigorous nervous tissue and brain capacity, and above all, that strength of character

which curbs irregular nervous expenditure. I repeat, if girls are to receive a higher culture, their physical education must precede any increase in their mental education. Without this the process cannot be safely effected, for the mental powers are developed in woman at a high physiological cost, which her feminine organisation will not sustain without more or less profound injury if bodily vigour go not hand in hand with it. It is more essential for a nation to produce lusty, vigorous offspring than to educate girls to the highest standard. By the highest physical education girls can be made strong, comely, and well-proportioned; while by the highest mental education (without this physical basis) they may be made into "blue-stockings," or neurotics, or both. By physical education I mean games and recreation which cheer and elate, not merely gymnastics and physical drill, which afford exercise without elation. These latter exercises are mainly for the sickly and deformed; and curative rather than animating. By physical exercise, too, I mean exercise taken out of doors; without this condition at least half of its value is lost. In wet weather dancing should be encouraged; graceful movements and carriage are only to be attained by means of well-developed springy muscles. Every educator of girls should feel disgraced by the lounging attitudes and awkward gaits which still prevail at many girls' schools, with their lop-sided shoulders and crooked backs; for in these is manifest the vicious system of education in vogue. Symmetry is of paramount importance in women for ensuring the production of healthy offspring.

While I hold that, subject to the restrictions I have laid down, girls may safely receive a higher education than has hitherto been accorded to them, I would urge that their moral education is of more consequence to themselves and the nation than their purely intellectual development. With a physical education such as is their due, we should, almost in a generation, eradicate the neuroses and anæmia to which at present girls are so prone; in their place we should perceive more even spirits and more stability of character, and the aping of man would give way to a more dignified respect for the qualities of their own sex.

It is now generally recognised that the school-room is the place to inculcate the *rudiments of physiology* in relation to health, with instruction in *personal hygiene*, or those laws of health which will assist the young in the management of their own health. But I deprecate the general teaching of anatomy and physiology to school children, as is the growing custom in Germany, not only on principle, but also because the child's curriculum is already overloaded. The elder girls should be instructed in some of the *duties of motherhood*, and the importance of breast-feeding to the mother as well as to the child; and thus remove the milk-question, which is answerable for such a large infant mortality, and which must be wiped out in these days of a diminishing birth-rate. They should also be taught *cooking* and food-values; and there are many other matters connected with the upbringing of girls to which their attention should be called early in life. They should be made to understand

the value of temperance to the adult, and of total abstinence to the child.

They should be familiarised with the fact that *tuberculosis* is more a *house-disease* than an infectious disease, and that it can be exterminated by fresh air in the home and in the school-room, and by cleanly habits. Teachers should receive an elementary knowledge of *infectious diseases*, with reference to their early diagnosis, and so minimise these diseases in the early years of childhood, when they are so fatal. They should also instil into their pupils the value of cleanliness, with a view to the prevention of *parasitic diseases*; and the meaning of *vaccination*, and how, when efficiently performed, it exterminates small-pox. By such knowledge disease is prevented, and a hardier race engendered.

I trust I have made it manifest that, to produce a sound human being, it is imperative that there should be a concurrent development of mind and of its physical basis during the period of youth. It is during these years only that we can educe faculties, form character, and invigorate the physical powers and functions. The school, where most of the years of youth are passed, is an epitome of the world at large,—a place in which to prepare the young, and not to unfit them, for their duties as men and women.

CLEMENT DUKES.

OLD AGE

By Sir HERMANN WEBER, M.D., F.R.C.P.; and F. PARKES WEBER, M.D., F.R.C.P.

Part I.—The Physiology and the Pathology of Old Age

By F. PARKES WEBER, M.D., F.R.C.P.

SPACE will not permit of a thorough discussion of all the characteristics of old age, many of which are probably too well known to need description here. In regard to anatomical, physiological, and medical characteristics it is very hard to separate what is merely due to senility from the results of disease. In the so-called deaths from old age, careful investigation would probably nearly always show that some disease, though clinically more or less latent, had been present at the last as the immediate cause of death. The longer life had lasted the greater the probability that there have been diseases in the past which have left traces in parts of the organism, either in the form of organic changes or disturbance of function. Many changes formerly described as senile are now recognised as results of previous disease. At one time, apparently, even the fibrosis connected with obsolete or quiescent tuberculosis of the pulmonary apices in old

persons was regarded as a senile interstitial pneumonia. Atheromatous and local sclerotic changes in the large arteries and heart may, like scars in various organs, be results of past syphilis and other infectious diseases. Diffuse degenerative changes, resulting from previous alcoholism, may be clinically and pathologically mixed up with senile changes. Diseases—whether they leave obvious organic changes behind them or not—may so affect the organism as in some way to impair vitality and give rise to premature degenerative changes. Special parts of the organism may be thus affected (the heart, arteries, joints, etc.), and an organ which has apparently recovered from an acute affection may nevertheless remain a *locus minoris resistentiæ*, and be more liable to subsequent disease and degeneration. A general disease like syphilis may sometimes so impair the vitality of certain parts of the body that at a subsequent period local degenerative changes, with or without chronic inflammation, occur. It is perhaps chiefly in this way that tabes dorsalis and general paralysis of the insane are connected with syphilis. Disease or functional insufficiency of one organ may lead to early degeneration in other parts of the body. Thus, renal disease and pulmonary emphysema may throw extra work on the circulatory system, and cause hypertrophy and subsequent degeneration of the muscle of the left and right ventricles respectively; thyroid insufficiency, which gives rise to the tissue dystrophy known as myxœdema, may possibly likewise occur in a minor form as a local senile degeneration, and then be a cause of general nutritional disturbance.

All these considerations have an important bearing on the subject of old age, and more especially on the subject of premature senility. We have to consider—(*a*) The natural characteristics, both anatomical (chiefly atrophic) and physiological (diminished functional activity), of old age; (*b*) the acute and chronic diseases and the injuries, as well as the results of past diseases, most commonly met with in old age; and (*c*) the peculiarities of reaction in old age towards diseases and injuries. These subjects are intimately allied to each other, and it will be most convenient to consider all of them together under the headings of the various systems and organs of the body, and then to formulate our main conclusions.

1. The Circulatory System, the Blood and Hæmopoietic Tissues.—The great importance of disease and degenerative changes in the heart, in regard to early impairment of the various functions of the body and premature death, has long been recognised. Probably, however, too exclusive a part in the production of many general disorders has been attached to changes in the circulatory system. The aphorism, "a man is as old as his arteries," is of course taken literally, if we reckon the age from birth, a truism and a platitude; but in the sense in which it was meant and is generally quoted, it is probably less true than "a man is as old as he seems," "a man is as old as he feels," and other sayings of the same class, which are true in the limited sense in which they were intended to be used. Many aged, prematurely aged, worn-out and decrepit

individuals show relatively little degeneration in their blood-vessels; whilst the arteries at the wrists may be prematurely thickened, and even tortuous, in otherwise healthy persons, especially those accustomed to use their arms for hard muscular work, who subsequently attain old age. Humphry (50) obtained information as to the arteries in twenty-nine reputed centenarians; twelve of them were stated to have "even" arteries; in the others they were visible, knotty, or tortuous.

In discussing the condition of the *arteries* in old persons, we are met by a great difficulty, namely, the vague use of the term "arteriosclerosis," which is practically a Greek rendering of Gull and Sutton's term, "arterio-capillary fibrosis." What is now generally meant by *arterio-sclerosis* is a hardening of vessel walls, chiefly affecting the arteries of small and medium calibre, more or less in all parts of the body. The change consists mainly in a diffuse thickening of the inner coat. The patchy changes of the inner coat, known as arterial atheroma, chiefly affecting the aorta and larger arteries, have likewise been described by some writers, especially in Germany, as arteriosclerosis. Dr. Savill qualifies the first change as *diffuse intimal arterial sclerosis*, but besides intimal sclerosis he includes thickenings or hardenings of arteries due to changes in the middle and outer coats, under the broad heading "arteriosclerosis." These he names "medial sclerosis" and "adventitial sclerosis" respectively, and maintains that changes in the inner and outer coats are often secondary to changes in the middle coat. The changes in arteries which chiefly concern us from the point of view of old age are:—(*a*) The ordinary arteriosclerosis, or diffuse intimal sclerosis. (*b*) The patchy changes of the inner coat, known as atheroma. (*c*) Diffuse hypertrophy of the muscular tissue in the media, which Dr. Savill terms "arterial hypermyotrophy," and includes as one form what might clinically be regarded as arteriosclerosis. (*d*) Diffuse calcification or "petrifaction" of the media, which may transform arteries of medium and even large calibre into rigid stony pipes.

Two or more of these conditions are often associated together in the same person. It is probable that they should all be looked on as complications rather than as essential features of old age, and it is unnecessary to do more than to refer to some of the main points regarding their supposed etiology. Statistics published on the relation of arteriosclerosis (diffuse intimal sclerosis) to chronic nephritis, alcoholism, syphilis, rheumatism, gout, acute infectious disease, mental and bodily over-exertion, over-eating, and old age, are unfortunately of very limited value, as different writers have had different ideas of what should be included under the term arterio-sclerosis. Probably all these suggested causes may play a part in the production of degenerative changes in arteries. From the acknowledged frequency with which aortic aneurysm depends on syphilis, it can hardly be doubted that atheroma of the aorta and large arteries must often be a result of past syphilitic lesions, and the changes observed in the aortic intima after enteric fever and other severe infectious diseases show that such diseases are probably not rarely primary causes of later atheromatous

patches in the great arteries. Yet there remain cases both of arteriosclerosis and atheroma where no cause can be assigned. Metchnikoff (65) has suggested that toxæmic conditions, produced by absorption of toxins from the large intestine, may be responsible for a certain number of such arterial affections. There is no evidence that chronic constipation, apart from over-eating and other insanitary factors, induces early arterial degeneration. Probably all chronic toxæmic conditions may lead to chronic changes in the blood-vessels. Doubtless, also, chronic excess of blood pressure from any cause may lead to changes in the arteries. It is now well known that the suprarenal glands normally throw a substance into the circulating blood which helps to raise and maintain the blood pressure. Josué, Rzentkowski, and others seemed to have proved that a relationship sometimes exists between hypertrophy and excessive functional activity of the suprarenal glands on the one hand, and arterial atheroma and arteriosclerosis on the other. Osborne goes so far as to suggest that the cause of the excessive blood pressure so frequently observed in the arteries of elderly persons, is that the vaso-constrictor and pressure-raising action of the suprarenal glands are in old age insufficiently opposed by the vaso-dilator properties of the thyroid secretion, and of the internal secretion of the testes and ovaries.

In regard to the etiology of diffuse *calcification of the middle coat of arteries* very little is known, but it may be regarded as a senile change in so far as it is due to a morbid deposit of calcium salts, generally during old age, analogous to that which takes place in the so-called senile calcification of costal cartilages.

Arterial hypermyotrophy in old age is doubtless intimately connected with the increase of the arterial blood pressure frequently observed in old persons. Yet it cannot be regarded as a typical characteristic of old age, a period of life when an atrophic change in muscular tissues is the rule. It is, doubtless, analogous to hypermyotrophy of the heart, and as we know that cardiac hypertrophy occurs as a compensatory change in cases of valvular defect, we must suppose that hypertrophy of the muscular coats of the arteries is also compensatory in some way, and arises in accordance with the general laws of vital action and reaction, even in cases where it is impossible to trace the whole chain of cause and effect.

Further discussion on the relation of arterial changes to old age we must refer to Dr. Mott's article on "The General Pathology of Nutrition." We may here, however, mention that obliterative arteritis, as distinct from arteriosclerosis, that is to say, the rather rare so-called "idiopathic" kind (true syphilitic arteritis in the central nervous system and elsewhere may, of course, be left out of the question), such as sometimes affects two or three extremities of otherwise apparently healthy males at about middle age or even earlier (especially Jews between the ages of thirty and forty years, of the poorer classes in London and large continental towns), has no connexion, as it has sometimes been supposed to have, with premature senility, though the same or a similar form of obliterative

arteritis likewise occurs as an occasional cause of gangrene of the lower extremities in elderly persons.

The minute cutaneous *veins* in old people are often abnormally dilated in various parts of the body, but this change is not confined to old age, and sometimes occurs even in youth, with or without obvious exciting causes. Great varicosity of the larger superficial veins when present in old persons has usually commenced much earlier in life. The tendency to slight œdema of the subcutaneous tissues, often manifest in the aged, has been attributed to the walls of the *capillaries* becoming more pervious to the outward passage of fluid from the lumen, but this explanation is open to doubt. Changes in the capillaries, retarding the flow of blood, almost certainly constitute one cause of the increased arterial blood pressure and the arterial hypermyotrophy often present in elderly persons.

Heart.—The only true senile change which occurs in the heart is a diminution in its size and weight. The individual muscle fibres become smaller, and often show an abnormal amount of pigment granules ("brown" atrophy of the heart). Owing to shrinkage of the whole organ the pericardial covering becomes relatively thickened and slightly milky in appearance (102). Similar changes, however, are not rare in the hearts of younger persons, who die from cancer or other wasting diseases. On the other hand, the heart in advanced age may show hypertrophy which must be regarded as compensatory to obstructive disturbance in the peripheral circulation, atheromatous disease of the cardiac valves, and similar factors. Atheroma of the cardiac valves and endocardium is analogous to atheroma of the large arteries, and nothing need be said on the subject of this atheroma. Disease of the coronary arteries may, of course, give rise to cardiac trouble in old persons, but the causes of coronary disease are the same as those of the arteries in general.

As we have already mentioned, the arterial blood pressure is often increased (Professor Allbutt's "arterial hyperpiësis" (1)) in later life. Renal insufficiency, excessive or relatively unopposed vaso-constrictor action of the suprarenal capsules, over-eating, alcoholism, gout, rheumatism, primary changes in the arterioles and capillaries retarding the flow of blood, and even, we believe, primary hypertrophy of the muscular coats of the arteries, have all been suggested as causes for this excessive blood pressure after middle life, and doubless most of these may be factors in the production of excessive blood pressure.

The pulse of old persons often owes its main features exclusively to excessive blood pressure and loss of elasticity of the vessel walls. It is often, owing to feebleness of the heart, abnormally frequent, that is to say, on relatively little exertion or in the absence of any special exertion; but in some old persons a condition of bradycardia arises, which is doubtless always to be regarded as a disease superadded to the senility.

The diseases of the circulatory system play a great part in the

pathology of old age. They give rise to thrombosis of arteries and veins, senile gangrene of the extremities, hemiplegic attacks, and other cerebral symptoms, due to localised lesions in the brain, resulting from hæmorrhage or thrombosis. They also doubtless give rise to many of the various paræsthesiæ complained of by old persons. Slight hæmorrhages from the kidneys, bladder, stomach, and other organs may, like senile cerebral hæmorrhage, be due to degenerative changes in the blood-vessels.

The *blood in old age* does not appear to be specially altered, though there is sometimes a certain degree of anæmia with a diminution of red corpuscles. This may constitute an occasional cause of the slight œdema in the subcutaneous tissues of the lower extremities often noted in old persons, to which we have already alluded. Of the *hæmopoietic tissues*, the bone-marrow in old persons is probably more extensively of the fatty kind than it is in persons of middle and early life; but where senile osteoporosis is in active progress the proportion of fat cells may be relatively diminished. Of course, however, the condition of the bone-marrow in the aged depends largely on the presence or absence of disease (pneumonia, suppuration), and other causes which produce a leucoblastic or erythroblastic reaction; for the reactive powers of the bone-marrow are not lost, though they must be diminished, in the aged. It must not be forgotten that ordinarily less demand is made upon the hæmopoietic functions of the bone-marrow in old age than in earlier life.

The lymphatic glandular tissues undergo a considerable involution earlier in life. Chronic glandular swellings are, as is well known, at least those of a non-malignant character, chiefly met with in childhood, and it is in childhood that lymphatic glandular tissue is most functionally active and most developed in relation to the volume of the other tissues of the body. The Peyer's glands in the small intestine are relatively atrophied in old persons, but it is unlikely that this fact explains their relative immunity from enteric fever, as has been suggested by some. It may be noted that the late Professor G. Rolleston (78) found two Peyer's glands, microscopically normal, in a man reputed to be a hundred and six years old, though no mesenteric glands were visible to the naked eye in the layers of the mesentery. The spleen generally becomes smaller in old age (senile atrophy), and often its connective tissue elements appear relatively in excess. The thymus gland, indeed, shows considerable atrophy at puberty, and is generally quite atrophied and reduced to a mere vestige in later life.

2. The Respiratory System.—A kind of atrophic emphysema is the only true senile change in the lungs, but owing to cardiac disorders this is often complicated with passive congestion. Senile calcification of the cartilages of the bronchi, trachea, and larynx may be compared to senile calcification of the costal cartilages. This condition, by greatly impairing the elasticity and mobility of the ribs, and thus making the whole chest-wall rigid, may constitute a serious complication of old age. Owing to these various causes, and to senile changes in the heart, the

respiratory movements tend to be more frequent and shallower in old age than in middle life, and their frequency is more readily increased on any exertion. The diminution in the amount of carbonic acid gas exhaled corresponds to the general reduction of metabolic activity in old age.

The tendency to relative increase of connective tissue in old persons is well illustrated by subacute and chronic inflammatory processes in the lungs, for instance, by pulmonary tuberculosis, if this be present. In advanced life a certain amount of bronchitis is very common, but acute lobar pneumonia is probably the most frequent of the immediate causes of death. The onset of pneumonia is often extremely insidious, and grave cardiac weakness may rapidly supervene without there having been much fever. Hourmann and Dechambre (46), quoted by Charcot, speaking of the aged inmates of the Salpêtrière Hospital in Paris, say: "The old women do not even complain of malaise; no one in the wards, neither guardians, servants, nor neighbours, perceive any change in their condition. They get up, make their beds, walk about, eat as usual; then they feel a little fatigued, sink upon their beds, and expire. This is one of the sudden deaths in old age at the Saltpêtrière. The body is opened, and we find a great part of the pulmonary parenchyma in a state of suppuration." This quotation serves also to illustrate the frequent "latency" of symptoms in acute infectious diseases of all kinds in old age: but latency of symptoms is not confined to diseases in the aged; it may, as is well known, occur in younger persons, especially in those whose reactive powers have become blunted by the degenerative effects of alcoholism.

3. **The Alimentary System and its Glandular Appendages.**—In this division it is particularly hard to separate the results of disease from what is simply a part of old age. With lessened activity of the body generally, less demand is made by nature on the functions of the digestive organs, but frequently in ordinary life, in the well-to-do classes at all events, rather more than less work is thrown on them, there being more time and opportunity for eating and drinking. It is no wonder, therefore, that morbid changes, such as hæmorrhoids, so frequently give rise to trouble in middle life, when growth of the body has ceased. Though decay of the teeth is a pathological process, which often has its maximum at a relatively early period of life, the toothlessness of old age must be regarded as normal to that period of life, when indeed, owing to lessened tissue change and lessened activity of the body generally, less food is required. A certain amount of sluggishness of the bowels is probably also natural, and may be regarded as a sign of diminished functional activity in the alimentary tract.

The digestive troubles complained of by some old persons may be attributed partly to imperfect mastication and insalivation of food, and partly to the diminished secretion of digestive juices, which, like diminished secretion of sweat and urine, is associated with the generally diminished functional activity of old age. Relative dryness of the

alimentary tract may likewise account for some of the constipation of old people. On the other hand, in regard to certain dyspeptic troubles, especially in individuals of the nervous type, the blunting of nervous susceptibility in old age, and the relative absence of hurry and excitement, have, as is well known, their advantage; but this advantage is often abused, so that a man in old age indulges too much in the luxuries of the table, who, at the most active period of his life, was prevented from doing so by lack of time and by dyspeptic conditions.

The *liver* certainly, and probably also other glandular appendages of the alimentary tract, often undergo a process of senile atrophy, accompanying the shrinkage of other parts of the body. This atrophy of the liver involves the glandular cells more than the connective tissue, the consequence being that the capsule of Glisson, owing to decrease in bulk of the whole organ, becomes somewhat thicker and milky in appearance, and in microscopic sections of the organ the interacinous fibrous tissue is seen to be relatively in excess as compared with the glandular cells of the acini. On the other hand, in old age, when there is chronic bronchitis, with emphysema of the lungs, or when for any reason the cardiac power becomes insufficient, the liver may be increased in size from passive engorgement. A true cirrhosis of the liver from alcoholism, etc., can always be distinguished from the fibrous increase in simple senile atrophy. Cancerous growths in various parts of the alimentary canal, pancreas, and liver carry off a good number of old persons; but the only certain connexion between old age and cancer in this and other parts of the body is that cancer in the digestive system, as elsewhere, often attacks the sites of chronic irritation, and is a disease of the involution period of life.

4. The Urino-Genital System.—The kidneys escape senile atrophy more often than other viscera, and when any atrophy occurs, it is often secondary to changes in the small blood-vessels of the glomeruli, etc. In this atrophy of the kidneys, however, as in senile atrophy of other viscera, the parenchymatous elements shrink more than the connective tissue framework, with the result that, though the capsules strip easily, the surface of the cortex is slightly uneven or granular. Cysts in the cortex, such as Harvey (43) found in "Old Parr," may probably occur in senile kidneys in the absence of any real interstitial nephritis.

Weakness of the vesical musculature may of itself give rise to trouble in micturition, but in men the most serious disturbance of this kind is due to enlargement of the prostate, for which, fortunately, operative relief is now often possible. Humphry (50) found that, out of thirty-three reputed centenarians, about whom information under this heading was obtained, the micturition was reported to be natural in twenty-five, and it was not stated to have been difficult or painful in any. "All this," he wrote, "is confirmatory of the observation that the prostatic and vesical affections, which cause the larger proportion of urinary troubles of advancing years in men, commonly manifest themselves about or before

seventy in those who are disposed to them, and do not, for the most part, permit the sufferers to attain great age."

The quantity of urine is somewhat diminished in old age, and the daily amount of urea and solid urinary constituents is less than in middle age. This is accounted for by the lessened functional activity of the body generally, and the resulting diminished formation of waste products from tissue catabolism. It is often noted by old persons that their urine less frequently deposits urates on cooling than it did at early periods of life. Phosphatic deposits, on the other hand, sometimes become more frequent. An occasional trace of albumin or sugar does not necessarily signify the presence of grave disease.

The menopause, with the climacteric atrophic changes in the sexual organs of women, usually occurs between the ages of forty-five and fifty years, though the time of onset varies considerably in different individuals. In men the incidence of senile atrophic changes in the sexual organs is still more variable, and even if we do not admit the truth of the reputed escapades of "Old Parr" after his hundredth year of age, it is certain that the testes may sometimes remain functionally active to an advanced age.

5. **The Nervous System and Special Senses.**—The convolutions and the brain as a whole, like the other organs, shrink in old age, and because of this diminution in bulk, since the brain is enclosed in an unyielding rigid case, a condition of passive external hydrocephalus ("senile hydrocephalus") arises *ex vacuo*. By microscopic examination degenerative changes in the cerebral cells (17, 94) have been observed. The mental powers sooner or later fail more or less. "*Claudicat ingenium,*" says Lucretius, and prolonged mental effort becomes impossible. In some cases, with or without special arterial changes, we may even speak of an "intermittent claudication" of the brain, analogous to that of the extremities, the blood-supply of which is partially cut off. With the general diminution of mental power the memory for recent events is often specially impaired. In extreme cases intellectual decay proceeds to actual "senile dementia." Though the neuroglia may be relatively in excess, typical senile brains never exhibit chronic inflammatory changes like those seen in the shrunken convolutions of general paralysis of the insane.

Intimately associated with true senile changes may be other alterations due to diseases of the cerebral blood-vessels: atheroma, stenosis, and thrombosis of arteries, foci of anæmic softening, miliary aneurysms, and cerebral hæmorrhage. Cerebral hæmorrhage has been called the "sword of Damocles," always suspended over the heads of old persons. We cannot stop to discuss senile epilepsy, recurrent attacks of "senile" hemiplegia, slight (or "threatened") apoplectiform attacks, and various motor symptoms, due to changes in the cerebral blood-vessels of old persons; neither can we here consider the various sensory symptoms, local anæsthesiæ and paræsthesiæ of the ordinary or special senses, due to similar causes. The brains of old persons occasionally show a great

number of small cavities (35), due to repeated small hæmorrhages or local thrombotic softenings. It is probable that many cases of "senile paraplegia" (*vide* vol. vii.) are due to ischæmic changes in the spinal cord, connected with partial or complete obstruction in the small vessels.

Certain symptoms in old persons, partly nervous in nature, such as muscular cramps, temporary muscular weakness, or paræsthesiæ in the extremities, may sometimes be due not to changes in the central nervous system, but to disturbance in the peripheral circulation, with or without any degenerative changes in the peripheral nerves.

Both the *nervous thermotaxic and the vasomotor mechanisms* become less responsive to stimuli in the aged. They react sluggishly, or even insufficiently, to the application of cold and to acute infectious diseases. The diminished response of the thermotaxic mechanism may partly, however, be due to the diminished metabolic powers generally, and the sluggish response of the vasomotor mechanism may be partly due to organic changes in the walls of the peripheral blood-vessels. One would suppose that the average temperature of the body in very old age would be generally slightly lower than in middle life; but the reverse has been maintained by some observers, and Charcot concludes that the normal temperature undergoes "no appreciable modification with the progress of age," unless indeed it be that the difference between the external (axillary) and internal (rectal) temperatures is found to be generally greater in old than in middle age. Charcot explains the fact that the average normal temperature remains at least as high, though the nutritive and metabolic functions become less active, by the alteration in the state of the skin in old age. In the senile skin the vascularity and secretion are diminished, and though the aged probably produce less heat than do younger persons, they probably also lose less both from the skin and respiratory passages. It seems, therefore, that the only important thermometric peculiarity in the aged is that to which we have already alluded, namely, the diminished febrile reaction at the onset, and the relatively apyretic course, of acute infectious diseases, such as pneumonia. In these diseases the axillary temperature may, however, sometimes be found normal, or even subnormal, when the rectal temperature shows the presence of decided fever.

The acuity of the sense of pain is generally somewhat diminished in the aged, and especially is this the case in regard to sharp, sudden pain and "spasmodic" attacks. Relative absence of pain is doubtless one of the reasons why attacks of cholelithiasis and nephrolithiasis and other ordinarily painful affections sometimes are almost "latent" in the aged. On the other hand, ischæmic conditions of the lower extremities, due to arterial disease in the aged, may be accompanied by great pain, and the pains of muscular rheumatism and rheumatoid arthritis may be severe.

The *special senses* likewise become blunted in old age, but this varies greatly in different individuals, hereditary influences and past diseases doubtless playing a great part. As a rule, the perception of taste and smell is blunted in the aged. Undoubtedly a great deal of "senile

deafness," or rather deafness in old persons, is due to disease, such as past otitis media, and especially chronic dry catarrh and sclerosis of the middle ears, and, therefore, indirectly also to rheumatism, gout, over-eating, alcoholism, and the various injurious circumstances recognised as occasional factors in the production of gouty conditions. There is, however, sometimes an apparently primary atrophy of the auditory nerves as the cause of progressive deafness in aged persons. Mr. Lake suggests that the diminished perception of sound by bone conduction is due to increased porosity of the bones in old age.

The Eye.—Hardening of the crystalline lens commences in childhood, and gradually increases through life. A result of this hardening of the lens is that the power of accommodation is lessened, and at about the age of forty-five years ordinary emmetropic persons generally experience difficulty in reading small print without the help of spectacles. This "presbyopia" is said to commence when the "near point" for clear vision, which in emmetropics at the age of ten years is seven centimetres from the eye, has receded to beyond twenty-two centimetres. The further progressive hardening of the lens leads in more advanced life to diminution of the refractive power of this body, and hence of the eye altogether. Thus in persons originally emmetropic it gives rise to a certain amount of "senile hypermetropia" after the age of sixty-five years.

Senile cataract is the result of a degenerative change in the lens superadded to the normal process of senile hardening. The relation of primary glaucoma to age is well known. It is rare before the age of forty years, and from that age onwards increases steadily in frequency until advanced old age, when statistical evidence is uncertain. Central choroiditis is a chronic inflammatory change in the macular region, which affects old people especially; and in them this obvious affection of vision has been called "senile central choroiditis." A gradual atrophy (usually bilateral) of the optic nerves, accompanied by progressive loss of sight, sometimes appears as an apparent primary change in old age.

"Arcus senilis" is due to a granular hyaloid degeneration in the superficial layers of the cornea, close to the sclero-corneal margin, but separated from it by a ring of clear corneal tissue. It is rare before the age of fifty, but has been known to occur in children, especially as a family peculiarity. It is not of much value as a sign or index of degenerative changes or premature senility in other parts of the body.

A minor trouble of old age is the epiphora due to the displacement of the punctum lacrymale by senile ectropion of the lower eyelids. This ectropion is the result of a senile relaxation of the tissues of the lower lid, which, by allowing particles of dust, etc., to settle in and irritate the lower conjunctival sac, often also gives rise to a condition of chronic conjunctivitis.

6. **The Bones, Joints, and Skeletal Muscles.**—The relatively small weight of the dried bones from old persons is the result of a process of thinning, which may be termed senile osteoporosis, and is to some extent analogous to the osteoporosis occurring in various condi-

tions of cachexia, and in limbs which for any reason have become immobile. In regard to senile osteoporosis in the ribs, Cornil (21) points out that the bony lamellæ, notably the subperiosteal lamella, become thinner, and the medullary cavities become enlarged. This process explains the great friability of the ribs in some old persons, and likewise, as Humphry (50) has shown, the peculiar liability of the aged to fracture of the neck of the femur. Disuse of a part from any cause doubtless increases the tendency to senile atrophy of bones, the normal amount of which, even if it does somewhat increase the liability to fracture, has the advantage of reducing the body weight to accord with diminishing muscular power.

A characteristic senile change is that in the shape of the lower jaw (50), due to the atrophy of the alveolar border which follows the decay and falling out of the teeth. The diminution in the size of the face in old persons is partly due to atrophy of the alveolar border in both jaws, and partly to the general atrophic process which affects the whole skeleton.

Ordinarily the calvarium becomes thinner and lighter, like the whole skeleton, but occasionally it is decidedly increased in thickness, and much heavier than natural, even when the bones of the face share in the general senile atrophy. This increase in thickness of the skull-cap is due to a deposit of bone in the interior, and Humphry (50) has suggested that it may depend on increased afflux ("ex vacuo") of blood, determined by the senile shrinking of the brain. It may accompany chronic shrinking of the brain from causes other than old age. It may perhaps sometimes be connected with abnormal adhesion of the dura mater.

A curious and not very rare condition of symmetrical circumscribed thinning of the parietal bones, generally regarded as a form of senile atrophy of the skull, has been described, with or without illustrations, by Virchow (1854), Maier (1854), Sauvage (1870), Meyer (1872), Féré (1881), Eve, Humphry (53), Ziegler, and others. Most examples have occurred in old persons, especially women; but Meyer mentions commencing atrophy of the parietal bones in a melancholic man, only forty-four years of age, and we have ourselves (97) met with a typical instance in a woman only fifty-five years old. She had had biliary cirrhosis and jaundice of four years' duration, and the condition in her case might perhaps be regarded as a premature senile change connected with her nutritional disturbance. In the same way brown atrophy of the heart, exactly similar to that found in very aged persons, may sometimes be met with in younger persons dying of cancer and other chronic wasting disorders. Humphry, who (52), in 1858, regarded the conformation as congenital, afterwards (53) (1890) thought that it was the result of senile changes. The condition consists in a symmetrical circumscribed depression, generally extending over a considerable area, with shelving edges, on the outer side of each parietal bone, due, as Mr. Targett pointed out in our case, to removal of the outer table over the affected area, and wearing away of the diploë, so that the inner table forms the floor of the depression. In extreme cases small areas of the inner table may also be

completely absorbed. In the Museum of the Royal College of Surgeons are Egyptian and other skulls showing this symmetrical atrophy, and the Cambridge University Museum possesses a large collection of such skulls. Hollander, who has collected a number of cases associated with melancholia, regards the condition as due to trophic influences accompanying the melancholic state. We regard it as due to a process of concentric lacunar absorption, accompanying senility or other chronic states of depressed nutrition.

Calcification of the costal cartilages, when it is sufficient to impair greatly the respiratory movements of the thorax, is a serious disadvantage of old age. This calcification of cartilages is a degenerative change which may occur long before old age is reached, and on the other hand may not always be present, in its extreme degree, even in very advanced life.

We have not space to enter here on the various changes in and about the joints of old persons due to gout, chronic rheumatism, and rheumatoid arthritis (osteoarthritis, arthritis deformans, and in the vertebral column, spondylitis deformans). Chronic senile gout (attacks of typical acute gout are, of course, rarer in old age) and rheumatoid arthritis of the small joints, and the variety of osteoarthritis of the hip-joints known as "morbus coxæ senilis," are the forms of joint affection which are most connected with the pathology of senility.

In the *muscles* of old persons C. O. Weber (95) found that the individual muscle fibres were reduced in size, but that relatively few of the smaller (growing) muscle fibres were to be seen. He thought, therefore, that "aplasia" of muscle fibres had much to do with senile atrophy of muscles. In the muscles, as in other tissues, the connective-tissue elements do not appear to atrophy to the same extent as the parenchymatous elements, but some of the apparent connective-tissue increase may be due to atrophy of fat-cells. Muscular rheumatism, lumbago, sciatica, and neuritis or neuralgia of various regions, especially of the extremities—to which many persons after middle life, especially gouty persons, become very liable—are probably often due to inflammatory conditions of the over-nourished ("relative over-nutrition" (96)) connective-tissue elements in and about the muscles and nerves ("Fibrositis" of Sir W. Gowers). "Rusting from resting" and over-nutrition doubtless often play a part in the causation of such troubles.

We must not discuss the various disorders which may arise in old age in the extremities, from the diseases of arteries of which we have already spoken. These disorders include recurrent cramp, severe pain, various paræsthesiæ, intermittent claudication, and, finally, senile gangrene.

Many authors (2, 51) have observed that after wounds and injuries the healing tendency is often satisfactory in senile tissues. Especially is this the case in regard to the union of fractured bones, and Humphry (50) has pointed out that the reason why union usually does not occur after fracture of the neck of the femur in old persons, is not that the healing power is bad, but that the two surfaces to be united cannot be kept together.

7. **The Skin and Cutaneous Appendages.**—Loss of fat accounts for a good deal of the shrinking of the skin in old age, but a senile atrophic change (a withered, sometimes slightly scaly, sometimes glossy appearance) is almost equally shown in old persons who have never had excessive subcutaneous fat, and associated with the senile diminution in cutaneous secretion there is a notable dryness of the skin. Similar changes in the skin may occur, much earlier in life, in the subjects of any chronic malnutrition or wasting disease. Old age and atrophic changes in the cutaneous capillaries associated with it bear directly on the liability of the skin to various affections. "Senile pruritus," when it occurs, is doubtless intimately associated with senile changes in the capillaries and in the nutrition of the skin and cutaneous nerve-endings; but it is probably often excited by toxæmic conditions, due to digestive disorders or faulty action of the liver or kidneys. Likewise connected with the atrophic condition of the skin is the tendency, frequently noted in old persons, to the formation of pigment spots and patches, warts ("senile warts"), and multiple pin-point capillary nævi. These minute multiple angiomata are frequent at all ages, but especially frequent in atrophic conditions of the skin. Some authors have considered their presence in unusual numbers to be of some value for the diagnosis of internal carcinoma, but investigation has not confirmed this opinion.

With regard to the connexion between senility and the occurrence of cutaneous carcinoma and rodent ulcer, the considerations referred to in our remarks on the alimentary system apply. The relative slowness of the progress of malignant disease in old age can frequently be observed when the skin is the part affected.

The nails often appear to be thinner and more brittle, or more fibrous in structure, in old age than in middle life, and sometimes become more opaque and longitudinally grooved. Longitudinal grooving of the finger nails is, of course, not at all confined to old age, and by some has been associated with a rheumatic or gouty family history.

Baldness of the scalp tends to appear in middle life, is often connected with seborrhœic conditions, and is only secondarily connected with senility. Even whiteness of the hair (canities), a typical phenomenon of old age, may, as is well known, be established much earlier in life, with or without such reputed causes as heredity, mental and physical shocks, and severe strains on the system. It may be quite unaccompanied by signs of premature senility in the body generally. Metchnikoff (63) attributes the removal of pigment from the hair to the action of cells, which he calls "chromophages." According to him these chromophages are special varieties of a group of migratory, chiefly mononuclear, cells, to whose phagocytic action he attributes not only the senile atrophic changes in the bones and parenchymatous elements of the various organs (muscles, liver, kidney, etc.), but likewise the atrophic changes and scleroses of organs occurring in chronic inflammatory and cachectic conditions. These phagocytic cells he terms "macrophages," to distinguish them from the "microphages," or the polymorphonuclear leucocytes,

which play such an important part in acute and suppurative inflammations. Metchnikoff (65) has even suggested the possibility of obtaining a special "cytotoxic" or "cytolytic" serum to exercise an antagonistic action on the macrophages, to be obtained in the same way as hæmolytic sera, which, when introduced into the circulation, destroy the red blood corpuscles. The question is, however, whether in old age the macrophages do not simply remove the feeble and decaying cells in various parts of the body, just as they englobe the imperfectly formed red blood corpuscles in the bone-marrow and lymphatic tissues in cases of pernicious anæmia.

Conclusions

We may, with the poet Herrick, and the French physician Reveillé-Parise, compare the normal course of the physical life with the daily course of the sun in the heavens—with its gradual rise, its meridian, and its gradual setting. Death is the natural result of birth—"Nascentes morimur, finisque ab origine pendet" (Manilius)—in the sense that the same laws which regulate the commencement and evolution of an individual life lead it normally on to gradual involution and termination; or, as Sir Michael Foster writes, "The future decline of the brain is probably involved in the early decay of the thymus." The *memento mori* rhyme, "As soone as wee to bee begunne, we did beginne to be undone" (Wither's *Emblems*, 1635, p. 45), an old English rendering of the line of Manilius, is literally true in the sense that some structures of the body (for instance, the thymus gland, in late childhood (L. S. Dudgeon)), no longer so much required, begin normally to undergo involution at an early period of life.

"Atrophy in function," if we may use the term, and atrophy in structure are the essential characteristics of old age. Atrophy in function is shown by loss in physical and mental power, and by sluggishness of reaction generally. Loss in weight and bulk of the whole body normally accompanies the local atrophic changes in structure which are connected with the waning of functional power of the various organs. Senile atrophy of tissues seems to be partly due to an active phagocytic or absorptive action, as shown in lacunar atrophy of bones, and partly due to a relative aplasia (deficient formation) of new elements, as shown in senile atrophy of the skeletal muscles.

In old age, as in most chronic inflammatory diseases, the process of shrinkage is generally more obvious in the higher ("parenchymatous" or "noble") elements of an organ than in the lower elements, which constitute the connective and fibrous framework of the body. In some positions the lower elements may actually increase in bulk; the calvarium of the skull may increase in weight and thickness. In bones affected by osteoporosis the increase of the fatty elements is doubtless largely "substitutional," serving to fill up the spaces. Yet, though a certain relative increase of the fibrous elements is normal in old age, any considerable

absolute hyperplasia must be regarded as pathological—that is, as the result of disease, and this certainly applies to all actual "scleroses" of tissues and organs. In fact, it may be supposed that normally atrophy proceeds on the whole fairly equally in all parts of the organism, the descent in old age coming gradually, smoothly, and peacefully. But frequently, especially in cases of "premature senility," certain organs or parts of the body are affected before the others, giving rise to compensatory hypertrophies and changes, really foreign to old age, in other organs and other parts of the body. More often, however, changes (other than simple atrophic) found in old persons, and often regarded as characteristic of old age, are the results of disease, *e.g.* atheroma of arteries, disease of the cardiac valves.

The relation of cancer to old age is not quite simple. That it is not merely a question of the diminished resistance of senile tissues is apparently shown by the fact that cancer often makes slower progress in aged persons than in persons attacked while still robust and almost in their prime of strength. In regard to its frequently relatively slow progress in old persons, cancer behaves somewhat like tuberculosis.

The resisting powers of old age, if on the whole sluggish, are fairly efficient in regard to many injuries; and this is especially shown, as Humphry and others have pointed out, by good union of fractures in long bones in most positions. There is, indeed, no tendency in old age, as there may be during enteric fever and other severe infectious diseases, for wounds to remain open and to show no reparative changes.

In regard to the reaction of the organism to acute infectious diseases, "latency" of symptoms is more frequent in old age than in youth and middle age. Sluggishness in reaction is especially remarkable with respect to fever, which may be very slight or even absent. Grave symptoms of an asthenic type heralding the approach of death often occur suddenly when the first part of the disease has given rise to little trouble and has almost entirely escaped notice. This probably is partly due to a blunting or dulling of the nervous centres in old age, whereby death occurs more quickly and with less pain and distress.

Inasmuch as most of the changes found in old persons are not the results of simple senile atrophy, but are due to disease or premature degeneration in various organs and tissues of the body, there is some justification in saying that what is commonly regarded as "old age" is really disease—"Senectus ipsa est morbus," said Terence, before Cicero wrote his famous *De Senectute*—and, like other diseases, one should endeavour to prevent the avoidable part by prophylactic treatment at an earlier period. It is this endeavour to substitute a normal old age, at the end of a long and active life, with its gradual, smooth, and peaceful descent, for early old age resulting from premature degeneration and disease, with which the second and most important part of this article is concerned.

F. Parkes Weber.

Part II.—The Prevention of Premature Old Age and the Prolongation of Life to its Natural Term

By Sir HERMANN WEBER, M.D., F.R.C.P.

What is the natural term? The life of every species of animal has its approximative limit, due to the circumstances in which it has been originally created. The opinion that life was of longer duration amongst the ancients than now is not proved. The great ages attributed to the Hebrew patriarchs need not occupy us here. The difficulties of verifying the statements of great ages in past generations are very great, and even the often-quoted ages of Henry Jenkins, Thomas Parr, and the Countess of Desmond are to some degree mythical. (W. Thom and T. E. Young.) We are satisfied with the statement of the Psalmist, that at his time the limits of life were 70 to 80 years; yet life is occasionally prolonged to 90 and 100 years and more, as we know from the accurate statistics of life insurance societies and from the General Register of England, where, according to a communication from Dr. Tatham, the superintendent of the Office, there were living in 1901—above 90 years of age, 9538 persons (3056 males, 6482 females); and above 100 years, 146 (47 males, 99 females).

By examining the circumstances in which persons have reached very advanced ages, we may to some degree learn the influences which contributed to their longevity. Amongst such people some have led injudicious lives; but they are only exceptions to the rule. After having carefully examined the records of over 100 long-lived persons, and many of these individuals personally, we have reason to state that the majority of them were temperate and were small meat eaters, led an active life, many a life with hard work, with great restrictions as to food and comforts; that most of them were early risers, that the majority of them had a joyful disposition, and that only a few of them were intemperate or idle. We must keep before our eyes the means by which the health of man is produced and maintained, and those by which it is usually deteriorated, since the former are likely to promote, the latter to prevent longevity. We are told by some people that the means and ways to prolong life are tedious, and that they prefer to enjoy fully the pleasures of life to an abstinence for the sake of a tedious old age; but the old age which we endeavour to promote is not tedious; on the contrary, it is generally associated with a fair degree of happiness, the enjoyment of mental and physical activity, and is terminated at last by an easy death. The manner of living which we suggest does not entail *privation* of all pleasures, but only *moderation*, combined with mental and bodily activity; while a life of indulgence often leads not only to early death, but also to various forms of suffering.

It is generally accepted that *heredity* exercises a potent influence on the duration of life, that those whose parents and ancestors were long lived may expect to live longer than the descendants of comparatively

short-lived ancestors. This rule ought to suggest to us the aim to transform by degrees, through proper management, families with short and average duration of life into long-lived families, and we have no doubt that this could be achieved by judicious manner of living and judicious marriages. Heredity is, however, not omnipotent either for good or evil. On the one hand, the members of long-lived families dare not rely too much on their privilege; while on the other hand, members of short-lived families may prolong their lives. We could give numerous instances of persons who, counting upon their presumed inheritance of long life, shortened their lives by self-indulgence or intemperance, and even more striking examples of members of short-lived families who have prolonged their existence by judicious living. In order to combat the tendency to short life it is essential to ascertain the cause of death of the parents and blood relatives, and to fight these causes by appropriate manner of living; the tendency, for instance, to dilatation of the heart, and to frequent attacks of bronchitis and dropsy from inherited weakness of the heart muscle, can be successfully combated by adopting from early life habits of great moderation and of physical exercise, comprising especially breathing exercises and graduated climbing; the tendency to tuberculosis may be combated by similar means; and not less so that to atheromatous and allied changes in the arteries. Almost every tendency to chronic disease can be counteracted. By investigating in each instance the inherited peculiarities, the individual constitution, mental as well as physical, the possible influence of habits and surroundings, and carefully appreciating all these points, we can almost always give advice to prevent disease and early death. It is necessary to recognise all the weak parts of the entire organism and to strengthen them, either directly or, if this be impossible, indirectly, by improving the condition of other parts of the organism. Above all things, we must bear in mind that *good air in and out of doors* is one of the most powerful factors in improving and maintaining health, and thus checking the tendency to disease.

Assuming that death from old age is caused by a kind of atrophy—similar to that from starvation—of the tissues and organs, connected with changes in the small blood-vessels and atrophy of the hæmatogenic organs, our aim must be to keep them as long as possible in a working condition, and to prevent atheromatous and other kinds of degeneration. We effect this by keeping them in *action*, as *inaction* leads to decay; and the various means of exercise, muscular and mental, offer the best means of action.

The physiological processes connected with exercise have been studied by Ludwig and his pupils, including especially Sir Lauder Brunton of London, Professor Mosso of Turin, and also by Dr. George Oliver of Harrogate. During the action of an organ the arterioles become widened, more blood flows into the capillaries and the lymph-spaces, more food and more oxygen are carried to the tissues, and at the same time the waste products are absorbed. As a result the muscle increases in size. The same is true of the brain and nerve centres. The increased afflux of

blood to the brain during the act of thinking is shown by the ingenious experiment of Mosso, who has demonstrated that when a man is placed in the horizontal position on a finely balanced table, the head portion of the table goes down during the act of thinking. With increased afflux of blood to the organs goes hand in hand the increased action of the arterioles and capillaries, which through this action retain their elasticity, are prevented from degenerating, and thus remain in a fit condition to nourish the organs. Simultaneously with the blood-vessels the heart is kept in a healthy state.

There is great difference in different persons with regard to the vital energy of the heart and blood-vessels. Many people are so constituted that their organs of circulation remain sound during a long life without any special stimulus, while in others they are apt to decay at an early period of life, unless they are kept under the action of a natural stimulus; and such differences are often found to be hereditary in certain families through several generations. As we have already stated, the best stimulus for the muscles and the organs of circulation is *exercise*. Sir Lauder Brunton (9), in his lecture on "Atheroma," describes how each contraction of the muscle drives the fluid onward, and how with each relaxation its tissue-juice and products of waste are sucked into the lymph-spaces and lymphatics. Dr. Oliver sums up as the result of his experiments that exercise—whether solely muscular or respiratory, or both combined—stimulates the fluid exchange between the blood and the tissue-spaces.

The most natural form of exercise is *walking*, the action of which on the organism is rather complex. The contraction of the muscles of the legs attracts blood from the heart through the arteries, and squeezes out blood from the veins towards the heart, which is forced to contract more vigorously and more frequently. By the increased contraction of the heart and the greater demand for oxygen, the respiratory movements are increased, and the nutrition of the lungs is improved. The circulation within the abdominal cavity is likewise accelerated, partly by the increased pumping action of the heart, partly by the increased contraction of the diaphragm and abdominal muscles; and all the organs within the abdominal cavity share in the improved circulation. In addition to these effects of walking we must take into consideration the increased exchange of fluid between the blood and the tissues; nor must we forget the increased nutrition of the muscles, which when kept at rest have a tendency to atrophy; now atrophy of the muscles is in many persons a cause and also one of the first signs of senility, and one of the principal factors in the loss of weight and the diminution of heat-production associated with senile decay.

The amount of walking necessary for the maintenance of health varies greatly in different persons, and even in the same person in different circumstances, from half an hour to two or three hours in the day. Persons in advanced age are mostly unable to take as much walking exercise as the young; but in this point, too, there are marked differences, and the keeping up of the habit exercises a great influence. The

same applies to the rate of walking. Some persons, especially corpulent women, are unable to walk more than a mile or a mile and a half in an hour; while others can walk three and a half or four miles an hour up to advanced age. For persons with fairly healthy organs of circulation and respiration, or with only slight dilatation of the heart, graduated uphill walking, as suggested by Professor Oertel of Munich, is better than always walking on level ground. The regular walking exercise ought not to be interrupted, in fairly healthy persons, by so-called bad weather; it ought to be taken in all kinds of weather, for the body soon becomes accustomed to this. Many persons say that they get chills or rheumatism if they go out in damp weather; but this is the case only at first, and once accustomed they will find that the vicissitudes of the weather, though not always agreeable, improve the health and protect in a great measure against colds and other illnesses.

Those who are still fairly vigorous ought to make a habit of taking once a week a longer walk—say from three to six hours—according to the individual strength; and the benefit of such a walk is increased by taking only a small amount of solid and fluid food during the walk, for instance a few plain biscuits and a good-sized apple or orange. The body loses a certain amount of weight principally in the form of water, combined, however, with some salts and excretory matter. By the increased removal of fluid and diminution of supply, the tissues are somewhat starved and enabled to take up fresh in the place of the used-up material.

Many people have the idea that by this increased amount of exercise the organism is worn out sooner than by rest; but the "wearing-out" view, provided the exercise is not excessive, but adapted to each individual, is entirely wrong, since the animal body is not a machine made up of dead material such as iron, wood, or leather, but is composed of living tissues, which by work are enabled to take up and assimilate a larger supply of fresh material, leading to constant renewal. Conversely, too much rest renders the tissues apt to decay sooner.

It has often been said that old people require and ought to take but little exercise. This, however, is likewise not quite correct; though it is true that over-exercise and over-fatigue are injurious to them. They ought to adapt their walks to their decreasing power; but they may and ought to walk as much as agrees with them, and ought to keep this up regularly, since otherwise they lose the habit and their powers decrease sooner. There is in this respect a great difference between the old and the young; the young can soon reaccustom themselves to long walks after considerable intervals, but the old man can do so only very slowly and as a rule imperfectly. The beneficial effect of long walks and of all exercise is heightened by being taken in the *open air*, for by it the skin, the nervous system, and the digestive functions are strengthened, and the resisting power of the organism to chills and other morbid influences is increased; and this *resisting power* is one of the great factors to longevity. Even independently of exercise, life in the open air is

most beneficial to delicate persons, whether in bath-chairs, open carriages, or open shelters or verandahs. Not tuberculosis only is prevented and cured by open-air life, but also a great many other ailments and weaknesses. As "walking without an object" is tedious to many persons, it is necessary to awaken and cultivate an interest in the surroundings of a walk. One of the means by which we have often succeeded in overcoming this difficulty is by advising such persons to keep dogs and walk for the benefit of their dogs.

Still more beneficial than the once-a-week increased exercise is the plan of taking once or twice a year a *walking or climbing tour of three to four weeks* in mountainous districts (cf. H. Weber (100)), which exercises an actually rejuvenising influence on every organ of the body from the brain to the skin. The action of the heart is in all persons tangibly improved, in some to an astonishing degree. Playing golf, cricket, racquets, shooting, and deer-stalking act in a similar way, but not quite to the same degree; deer-stalking, when associated with climbing of steep mountains, comes nearest to it.

This remarkable improvement in the nutrition and action of the heart seems to be caused to a great extent by the deep inspirations which are induced by steady climbing. Many years ago, therefore, we turned our attention to *respiratory exercises.* As in walking and other bodily exercises, the amount and method of respiratory exercises ought to be adapted to each individual. It is often injurious in cases of great weakness of the heart, after pneumonia, pleurisy, rheumatic fever, etc., to begin at once with forced respiratory movements. We have generally commenced with only moderately deep inspirations and expirations made during about five minutes twice a day, and have gradually increased the duration of the exercises and the depths of the single acts. We usually advise patients to inspire in the erect position with raised arms and closed mouth, and to bend down during expiration, so that the fingers touch the ground or the toes. By degrees it becomes possible to make several up and down movements and circular movements with the arms during inspiration, and to bend and raise the body several times during expiration. By this alternate bending and raising of the body we gain the additional advantage of strengthening the lumbar muscles, and thus counteracting the tendency to lumbago. This advantage is likewise obtained by turning the body round the axis of the spinal column alternately, with the deep inspiration from right to left, and with expiration from left to right. By these movements we further bring into action the muscles of the neck and spine, and to some degree prevent the tendency to stiffness of the neck and spine, and the stoop so common in old people. Other combinations of muscular and joint-movements can be arranged according to the nature of the individual requirements; but the attention to other movements must not lead to neglect of the respiratory movements themselves, for to them the beneficial effect on the heart and lungs is due. They keep up the nutrition and efficiency of the lungs which in old age undergo a kind of atrophy, producing senile emphysema. At the same

time they maintain the elasticity of the chest walls, which are apt to become stiff, and thus to interfere with the free movements of the lungs and the pleuræ. Deep respiratory movements constitute also a kind of massage of the thoracic walls, the lungs, pericardium, and heart; and promote the important fluid exchange between blood and tissues already alluded to.

We must not be satisfied, however, with the few minutes devoted to these daily formal respiratory exercises, but must inculcate a habit of taking several times a day, especially while walking, deep inspirations and expirations.

Some people think these respiratory exercises tedious; but the benefit in health produced by them is so great that the sacrifice in time is small in comparison. We have often seen that persons who got out of breath from short walks and climbs improved very rapidly when they gave these exercises a good trial; they became able to take long walks and to do satisfactory mental work, and so outlived by many years all their brothers and sisters. They are especially useful to literary workers, statesmen, professional men, and others who are prevented from taking much active exercise. The most convenient times for taking them are in the morning before or after the bath, when the body is loosely covered with flannel, some time before dinner, and before going to bed.

We have already alluded to several other useful forms of exercise, and might mention many more, such as P. H. Ling's Swedish exercises, the so-called Danish exercises, Streber's gymnastics, the usual German gymnastics (Turnen), and others more or less generally known; but we cannot enter here on their methods. We must, however, say a few words about an efficient and easily practised form, recommended by Dr. G. Oliver, the *static* or *tension exercises*, which consist in the static contraction of all the muscles of the limbs and trunk during one or two minutes. They are especially useful in *goutiness*, in which the arterial pressure is increased and the tissue-fluid, prevented from completely returning to the blood, lodges in the tissue-spaces. Dr. Oliver finds that one minute's tension clears up as much as 20 per cent of lymph. These tension exercises are most conveniently practised an hour before each meal, when nature produces a normal fall in the arterial pressure. (See also article on "Exercises," p. 403.)

The *digestive system* and *food* require the same attention as the circulatory system. It is impossible, however, to give rules suitable to every one, since the peculiarities of different persons are great and require individual attention. One rule, however, we may lay down with safety, viz. that great moderation in the amount of food ought to be practised by every one, especially with regard to the most nourishing articles of food (proteid food, including fish, eggs, and pulses), and that this rule applies particularly to the aged. Many persons have very erroneous views on this subject; they think that a very large amount of nourishing food is required to do active, mental, or muscular work, and that health and strength cannot be maintained without it; but careful

observation is not in accordance with this view. Amongst the results of the investigations of the "Collective Investigation Committee," we find that only 5 per cent of the persons above eighty years of age had been large eaters of animal food, and that the majority had taken small quantities of meat. This is also the result of the experience of Dr. George Keith (56), of Sir Henry Thompson, and of Dr. A. Haig. One of the most instructive treatises on this subject is that by L. Cornaro of Venice, who, at the age of ninety, describes his own manner of living, and how, by adopting it, he regained health after he had been in his younger days a sufferer from want of attention to diet. Sir William Temple, in the chapter on "Health and Long Life," says that essentials amongst primitive people are—"great temperance, open air, easy labour, little care, simplicity of diet, rather fruits and plants than flesh." On the subject that in old age the amount of food ought to be restricted, Dr. George Cheyne says "the aged should lessen the quantity and lower the quality of their food *gradually* as they grow older—even before a manifest decay of appetite force them to it." The opinion which many people hold that meat is necessary for a fair amount of physical or mental work is disproved by the fact that the Japanese, who excel in both, take, as a rule, no meat, but only a moderate amount of fish and eggs with rice, vegetables, and fruit; and further, by the experience that vegetarians have frequently beaten meat eaters in gymnastic competitions.

Vegetarians, strict as well as modified, often attain very long lives, and can perform good mental and bodily work; but we have not been able to convince ourselves that in the majority of fairly healthy people a moderate quantity of animal food is harmful, although in gouty persons and in old people the amount ought to be very limited, and green vegetables ought to be substituted for it. On the other hand, we have found that in persons accustomed to a preponderant meat diet, the continued attempt to accustom themselves to an exclusively vegetable regime leads to various digestive disturbances which are removed by reintroducing a small quantity of animal food. Many persons entertain the erroneous view that loss of weight in old age is an indication that more food ought to be taken; but in the majority of cases, unless the emaciation is very great and sudden, this is a mistake. Ample observation has shown us that most healthy persons do not increase, but slowly decrease after 70 or 75, and that increasing corpulence is not good, and ought to be counteracted by the quantity and quality of food and other means, especially if it is an impediment to the proper amount of active exercise. The old saying, *corpora sicca durant*, is quite in accordance with our experience.

The public often asks for rules about the quantity and quality of food. It is, as already said, impossible to give these in a satisfactory manner, since there is a great difference in the requirements of different persons according to the conditions of their bodies, their weight, the proportion of muscle to fat and bone, their age, the amount of mental and physical exercise, the meteorological surroundings, the climate, and

other matters. Rules can only be good when adapted to each individual. We will, however, give a rough estimation of the requirements of a man of middle age, living in a temperate climate, weighing about 150 pounds, measuring about 5 feet 9 inches, who walks about six miles a day, and is occupied six or seven hours with mental or office work :—

Milk, 30 ounces; cooked meat, 6 to 8 ounces; bread, 16 ounces; potatoes, 6 ounces; green vegetables and fruit, 16 ounces; butter, $1\frac{1}{2}$ ounces; salt, $\frac{1}{4}$ ounce; water, 50 ounces, a great part of which may be consumed in the form of tea, coffee, chocolate, soup, wine, or beer.

In this list fish, poultry, game, and cheese may be substituted for meat, taking into consideration that an ounce of cheese contains more nitrogenous food and less fluid than the same weight of meat; in the same way farinaceous and bread puddings may take the place of potatoes, lard or the fat part of bacon that of butter. Very useful and beneficial articles of food, especially for gouty people, are buttermilk and sour milk, which, as Metchnikoff has found, diminish the amount of the injurious microbes swarming in large amounts in the colon.

The allowance is ample for a middle-aged man with only moderate physical work; but during the period of rapid growth and development, say from fourteen to twenty years of age, boys occupied with lessons and active games or gymnastics require more food, and especially more meat; this also applies to girls between the ages of twelve and eighteen years, if they take as large an amount of physical exercise as they ought to do. On the other hand, persons approaching the period of old age, say from the sixtieth to the seventieth year, ought to be satisfied with about three-quarters of the ration mentioned, and after seventy with two-thirds and less, and especially with a much smaller proportion of meat. We, however, speak only of the rule, which allows many exceptions due either to peculiarities of constitution or to special occupation and climatic influences, or to increased or diminished work. Thus, for instance, soldiers on heavy duty, labourers performing extra work, require more than the average given; even old men doing an unusual amount of labour, bodily or mental, or both, require rather more than those who rest. On the other hand, persons taking no or very little exercise require less food in proportion to the same body weight. The proportion of different kinds of food ought to be arranged, not only according to the weight of the body and work done, but also, as already incidentally mentioned, according to the proportion of muscles to the rest of the body. The waste in nitrogenous matter of a large mass of muscles is greater than that of a small mass, and hence the body with large muscles requires more nitrogenous food to supply this waste and to maintain the equilibrium. The degree of activity of the nervous system has likewise great influence; while the shape of the body must be taken into consideration, since a long and thin body loses for the same weight more heat by radiation than a short and round one. In cold climates and cold weather more food is required than in warm climates and warm weather, and there is greater inclination for fat, especially lard, bacon, and butter.

The distribution of the food during the twenty-four hours can be varied considerably according to the constitution, the nature of the occupation, and the social habits. Many strong and healthy persons feel best with only two meals, viz. a good breakfast and dinner, or early lunch and dinner. Others require three meals: breakfast, lunch, and dinner; others four, viz. breakfast, lunch, tea, and dinner, or breakfast, dinner, tea, and supper; and again others even five, more especially during convalescence from acute disease.

It is, however, not only the quantity and quality of the food on which the health of man depends, but to a great degree also the *manner in which it is taken.* Above everything it must be *thoroughly masticated.* From time immemorial this has been preached, and many intelligent men (the late Mr. Gladstone, for instance) have tried to instruct their friends on this important point, but few people carry out this advice. Dr. van Someren, Mr. Horace Fletcher, and Dr. Harry Campbell (13) deserve, therefore, our thanks for having forcibly and intelligently urged the necessity of proper mastication. Much less food is required if it is thoroughly masticated than if it is bolted; great saving of expense could be obtained and many diseases could be avoided.

Another rule ought also never to be forgotten, namely, that food ought not to be taken while the mind is in a state of anger or worry, or while the nerve force is exhausted from mental or physical over-work. Rest of mind and body ought to precede the meal in such conditions.

The preparation of food, *i.e.* the cooking, is likewise of great importance, since it ought not only to render the food easily digestible, but also palatable, for the nerve influence and, through this, the secretions greatly depend on this.

Amongst food accessories *alcohol* and *alcoholic* stimulants are quite unnecessary to the great majority of people, but are harmless to many if taken with great moderation, and even useful in some conditions of exhaustion or weakness of the heart, of advanced age, but even then only in small quantities. The great majority of long-lived persons are either abstainers or very temperate drinkers.

Tea and coffee are likewise not necessary for the maintenance of health, but are agreeable excitants, and are therefore useful if taken with moderation. *Cocoa* is less excitant and contains more nutritive material, but can scarcely be considered valuable as food.

The important function of the *action of the bowels* is in many persons quite regular without any thought or management on their part; in others there is a constant tendency to constipation, in others to diarrhœa. Constipation is often caused by a certain torpor of the intestines; the ordinary kind and amount of food does not sufficiently stimulate them; they require some slight mechanical irritation to promote peristalsis, such as is caused by the bran in the whole-meal bread, or the fibrous portion of green vegetables, which lead to a more bulky motion, while a preponderance of flesh food in the diet, which is in great part

absorbed, is not suitable to them. Massage of the bowels and the methodic contraction of the abdominal walls (abdominal pressure) are likewise useful, as well as education of the bowels to regularity in this function.

Not less important for longevity than the systems of circulation and digestion is the *nervous system*, which governs all the other systems and is inseparable from them. As the state of nutrition of the nervous system depends on the supply of blood and the condition of the arterioles, we must endeavour to keep these effective by a sufficient supply of blood. Degeneration of the blood-vessels of the brain, leading to thrombosis or hæmorrhage, is a frequent cause of premature death, and although to a certain degree hereditary, can in most instances be prevented by great moderation in food and stimulants, regular physical exercise, and judiciously arranged mental occupation. The arterioles supplying the brain and spinal cord profit like all the other organs of the body by regular physical exercise, since through the increased action of the heart the nutrition of the arterioles is promoted, and simultaneously that of the nerve substance. Mental work causes an increased flow of blood to the brain, as shown by Mosso's ingenious experiment previously mentioned, and this tends to maintain the healthy condition of the arterioles and the substance of the brain, and to prevent early death. Mental work is, in fact, a promoter of a long and happy life, and steady mental work is not likely to wear out the brain too soon, just as little as steady physical exertion wears out the organs of locomotion and circulation. We often hear that with the approach of old age mental occupation ought to be greatly diminished, but this can be accepted only with considerable limitations. It is true that mental overwork ought to be avoided by the old as well as by the young; but a fair amount of work ought to be made a habit, and the longer this can be kept up the better. The custom of retiring from public appointments at the age of 60 to 65 may be necessary on public grounds, but unless some other work is substituted, it is often injurious to the individual. History and biography give us abundant proof that mental activity can be continued by great men up to very advanced age to their own benefit and that of humanity. Cicero says, very justly, that "the intellectual powers remain in the old, provided study and application are kept up, and old age need not be inactive, indolent, and drowsy."

Those who have no fixed occupation must find work for themselves, social, philanthropic, and so forth, and especially in old age a hobby. It would be easy to give many instances to show that in families predisposed by heredity to early death from the brain, this can be warded off by proper exercises of mind and body, associated with moderation in food and stimulants.

The health and, indirectly, the duration of life are greatly influenced by the *tenor of the mind*. Equanimity, contentedness, joy, happiness, hopefulness, satisfaction with one's surroundings, act as health producers; while mental irritability, envy, discontentedness, repining, and worry act

as the most depressing agents on mind and body. The cultivation of cheerfulness, the checking of irritability, envy, and anger, the strengthening of the sense of duty and of the will to carry out what one considers as right, even at the sacrifice of momentary advantages, exercise a most beneficial influence on health, and thus promote old age with happiness; while the opposite, especially the consciousness of neglected duty, leads to mental depression, to disease and shortening of life, or sometimes to a wretched instead of a happy old age.

An important function of the brain, *sleep*, does not receive sufficient consideration by most people. The amount of sleep required varies very greatly according to age, occupation, and habit. Children require much sleep, but the time required diminishes from early infancy to adult life. During the first months of life 18 to 20 hours is not too much; at the age of two years 12 to 14 hours is mostly ample, from the sixth to the tenth year 10 hours is generally enough; from the eleventh to the sixteenth 8 to 9; and after this age 6 to 8. Many persons fall asleep as soon as they are in bed, and sleep through without waking; others lie awake for some time; others, again, wake very often, and thinking this to be very injurious to them, take refuge in soporific drugs. If this is done but rarely, no great harm results, but if it is frequently repeated and becomes a habit it is injurious, although the nature and dose of the drug make some difference.

The fear, however, that lying some time awake, or waking frequently during the night, is very injurious to health, is always exaggerated and in most cases entirely unfounded. We are acquainted with many persons who from early periods of their lives have been poor sleepers, have scarcely ever slept a night through, have throughout adult life rarely had more than 5 to 5½ hours' actual sleep during the 24 hours, but generally less, and yet have lived to 75 years and more, and have retained their faculties in a remarkable way.

The habit of sleeping much, viz. over 8 hours, is often more injurious, and shortens life more frequently than sleeping only 5 hours, since it causes diminution of the activity and elasticity of the arterioles of the brain, and, in consequence, a tendency to thrombosis or hæmorrhage, or early degeneration of the mental faculties. The time for sleep is the night, and the habit of going to bed after midnight and sleeping to late hours in the morning is injurious to health and therefore to longevity. It is a bad habit to work or to devote to social amusements the greater part of the night until midnight, or 1, 2, or 3 in the morning, and then to remain in bed till 9 or 10 or later. Many literary persons say that they cannot work so well in the morning as during the first part of the night, or that they become exhausted when working early in the morning; but this is only the consequence of a bad habit, and if, on rising early, they would take a cup of milk, or weak tea, or water with a piece of bread, they would gradually become accustomed and work better in the morning than in the evening, and this with an improvement of health. John Wesley, it is stated, rose for sixty years

every morning at 4 o'clock, and never slept more than 6 hours. He led a most active life until his death at 88 years of age.

Health and duration of life are greatly influenced by the *cutaneous system*, the functions of which are not only excretory, but are amongst other actions intimately connected with the regulation of temperature and with the protection of the body from external influences. The skin is apt to share in the process of atrophy associated with old age; some of the capillaries and glands become obliterated, the skin becomes drier, and in many persons rather parchment-like. All kinds of active exercise, especially steady walking, send more blood to the skin, improve its nutrition, and through this prevent or at all events postpone the process of atrophy; but one of the most powerful means is *the bath.* The manner of using the bath and allied agents must, however, be adapted to the varying conditions of different individuals. The majority of fairly healthy persons are able to take a cold bath every day and greatly benefit thereby; and many with a fair circulation can continue this to very advanced age; others, however, with a weak circulation must be satisfied with a warm bath. Others do well by beginning with a warm bath, and letting cold water flow in afterwards and sluicing themselves, head included, thoroughly with cold water at the end of the bath. If the cold bath cannot be managed, a hip bath, or rubbing the body with a wet, rough towel may be substituted. The active rubbing and drying of the body after the bath is of great value; it acts like a kind of massage to the skin, and necessitates, if properly done, slight gymnastics of the arms, which are not sufficiently exercised by most people, and ought to receive more attention, in addition to the movements which, in the earlier portion of this article, we have suggested in combination with the breathing exercises. The hardening effect of the bath can be increased by keeping the naked body, after the drying process, exposed for 5 to 15 minutes to the air, before dressing, and the advantage of this *air-bath* will be increased by active movements of the arms, legs, and trunk. Helpful in keeping up the function of some organs are different forms of *massage*, which almost every one can practise on himself; thus we may mention massage of the eyes, ears, and nose, massage of the thyroid gland and of the scalp, as beneficial.

Amongst the agencies which influence the body and can be made to assist in prolonging life we must not forget *climate.* With increasing years the power of adaptation of the body to resist inclement meteorological influences decreases in some more, in others less; and it is prudent for old persons, who during the cold and stormy season are apt to suffer from bronchitis, rheumatism, or inability to keep up their body warmth and cheerfulness, to migrate to warmer and more sunny climates, where they can be during a great part of the day in the open air, exhilarated by the flowers and the blue sky. To avoid disease is a very important item towards attaining a long and healthy life, not only with regard to climatic influences in old people, but with regard to all other injurious influences throughout life. A regular *change* is useful during all periods of life, but

particularly so to old people whose mental activity begins to be stagnant; and to these the advantages of the change are enhanced by visiting localities where their attention is stimulated by art, by monuments, by history and antiquity, by scenery, and by the manners of the people. Speaking of climatic and meteorological changes, we must urge the necessity of the adaptation of clothing to the external influences. It might be thought that this is self-evident, but we must never trust in matters of health, or indeed in any other matters of importance, to the idea that the essentials are self-evident.

In reviewing the suggestions contained in this article towards attaining old age associated with happiness, it will be seen that we possess no master key, *no arcanum*, but that attention must be directed to many points, which not rarely are considered either unimportant, self-evident, or too tedious to be carried out, but the attention to which nevertheless exercises a powerful influence on the health, happiness, and efficiency of man.

We may sum them up in a few rules:—Moderation in eating, drinking, and physical indulgence. Pure air in and out of the house. The keeping of all the organs of the body in working condition. Daily regular walks in all weathers, supplemented by breathing exercises, walking and climbing tours. The aim to increase the resisting power, and through this avoid disease, and counteract inherited tendencies to various diseases. Regular work and mental occupation. Cultivation of equanimity, cheerfulness, and hopefulness. The training of the great powers of the mind in the path of duty in all concerns, and the control of anger, envy, jealousy, and every other kind of passion. Daily baths or ablutions of the whole body. The keeping of early hours in rising and in going to bed, and the restriction of the hours of sleep to 6 or 7.

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DIETETICS

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I. The Physiological Principles of Dietetics

By R. Hutchison, M.D., F.R.C.P.

1. The Functions and Nutritive Constituents of Food

Food fulfils two functions in the body: (1) It provides for the formation of new tissue for the repair of the waste which is constantly going on; (2) it supplies the raw materials for the production of energy to be expended in the form of heat and work. The former of these functions provides for the conservation of matter in the body and for the requirements of growth; the latter provides for the conservation of bodily energy.

The chemical ingredients of a food, in virtue of the possession of which it is able to accomplish these functions, are called its *nutritive constituents*, and are as follows:—

(1) Proteids, *e.g.* myosin in muscle, albumin in egg-white; (2) carbohydrates, *e.g.* sugars and starch; (3) fats, *e.g.* butter fat and vegetable oils; (4) albuminoids, *e.g.* gelatin; (5) mineral matters, *e.g.* common salt, phosphates; (6) water.

Most natural foods contain additional ingredients, such, for example, as flavouring materials of one sort or another; but the "nutritive constituents" are the only components of any importance for purposes of nutrition, and unless a substance contains one or more of these it is not, in the scientific sense, a food at all.

The requirements of nutrition are met in different ways by the various groups of nutritive constituents. The formation of new tissue and the repair of bodily waste can be carried out by the proteids, mineral matters, and water, and by these alone—all of them are necessary for the purpose. On the other hand, the proteids, carbohydrates, fats, and albuminoids are all capable of liberating energy in the body; whereas the mineral matters and water are of no use for that purpose. Proteids are thus the most important of the nutritive constituents of food, for they alone are capable, not only of repairing tissue waste, but also of serving as sources of energy. Lean meat contains proteids and mineral matters in abundance, and hence it is that life can be maintained on a diet of lean meat and water without any other addition.

2. The Relative Value of Foods

(*a*) *As a Provision for Growth and the Repair of Tissue.*—The richer a food is in proteids and mineral matters the greater its power as a potential tissue-former. In order to judge of the relative value of different foods

from this point of view, then, all that is necessary is to know their percentage composition (see tables of analysis below). The animal foods as a class, being rich in proteids, are more valuable as tissue-formers than the vegetable foods, most of which are comparatively poor in that constituent; but even some animal foods, such as butter, contain no proteid, and are therefore worthless from this point of view.

(*b*) *As Sources of Energy.*—In order to compare the value of different foods as sources of heat and work, some standard is required by which to estimate the amount of energy they are capable of yielding. The standard employed for this purpose is the large or kilo-calorie, *i.e.* the amount of heat required to raise the temperature of one kilogramme of water 1° Centigrade. Now, it has been found by experiment that the amount of energy which a food can liberate when oxidised inside the body is exactly equal in calories to the amount of heat yielded by its complete combustion *outside* the body. It will be obvious that by burning up a given weight of any food in a suitable apparatus, and measuring the amount of heat produced in terms of calories, we are in possession of a means of comparing the relative values of foods as sources of energy. The following table represents the results of such an experiment with some typical foods:—

Amount of Energy (in Calories) yielded by the Complete Combustion of One Gramme of Various Foods.

Bacon	8·8
Butter	8·6
Rice	3·5
Peas	3·3
Fat beef	3·2
White bread	2·7
Cheese	2·4
Egg	1·5
Potatoes	0·9
Milk	0·7
Apple	0·5

For practical purposes, however, it is more convenient to calculate the caloric value of a food from the results of its analysis into its different components. Careful experiments have shown that the amount of energy yielded in the body by the ingestion of one gramme of each of the chief nutritive constituents of foods is as follows:—

Proteids	4·1 calories.
Fats	9·3 ,,
Carbohydrates	4·1 ,,

If, now, the percentages of nutritive constituents contained in any given food be obtained by chemical analysis, it is an easy matter to calculate the amount of energy which a given weight of that food is

capable of yielding in the body. It is in this way that the "energy-value" of a diet is usually estimated.

The richer a food is in fat the greater is its value as a source of energy, for a given weight of fat yields more than twice as much heat on combustion as an equal weight of either proteid or carbohydrate.

(c) *As regards Digestibility.*—By the "digestibility" of a food is meant the time occupied by its digestion in the stomach; we have no means of estimating with any accuracy the relative length of time occupied by the digestion of different foods in the intestine.

The mechanical form and consistency of a food influence, more than any other factors, the ease with which it can be digested in the stomach. The more compact a food is, and the greater the amount of solid matter it contains, the longer is the period during which it remains in that organ. Leube divides foods into four groups, according to the ease with which they are digested, the first group containing the most digestible:—

1. Beef-tea, slightly cooked or raw eggs, milk, biscuits.
2. Sweetbread, boiled fowl or pigeon.
3. Scraped underdone beefsteak, potato purée, stale bread.
4. Roast chicken or veal, cold roast-beef (underdone), white fish, macaroni, rice, chopped spinach.

The following results of Verhaegen are also of interest:—

½ litre of boiled milk leaves the stomach in . . .	2½ hours.
1 " " " " . . .	3½ "
100 grammes of bread leave " . . .	3 "
150 " " " " . . .	4 "
100 " " and 60 grammes of meat leave the stomach in	4 "
An ordinary dinner leaves the stomach in . .	4 to 5 "

(d) *As regards Absorption in the Intestine.*—The degree of completeness with which a food is absorbed in the intestine is of the greatest importance in determining its relative value as a source of nutriment. Of the different nutritive constituents of food the fats and carbohydrates are the most completely absorbed; the loss of proteid is always considerably greater. Especially is this the case as regards the proteid of vegetable foods, the absorption of which is apt to be seriously interfered with by the cellulose in which it is enclosed. Thus on a purely animal diet there is but little proteid lost; but when vegetable foods are taken alone the waste is very considerable, amounting, in the case of carrots, for example, to 40 per cent of the total proteid consumed. In general terms it may be said that the components of a mixed diet are more fully absorbed than those of any one article of food when taken by itself. In the case of an ordinary diet the following may be regarded as the percentages of the different nutritive constituents which will be absorbed: proteids, 92 per cent; fats, 94½ per cent; carbohydrates, 98½ per cent.

In such a condition as diarrhœa, a study of the relative capacity for absorption of different foods is of value in enabling one to select a

diet which will leave as small a residue as possible in the intestine. Decoctions of foods which consist mainly of starch, *e.g.* rice, arrow-root, and corn-flour, best fulfil this requirement. In constipation, on the other hand, where it is desirable to leave a large amount of unabsorbed residue in the bowel, one would select such articles as green vegetables and fruits, the cellulose of which the human intestine is almost incapable of absorbing. It should be pointed out that even in health anything approaching complete absorption of the ingesta is not to be wished for; a moderate residue is required to act as "ballast" and to help in stimulating the peristaltic movements of the bowel.

(*e*) *As regards Cost.*—In constructing dietaries for the inmates of public institutions, and in judging of the suitability or otherwise of the habitual diet of the poorer sections of the community, the relative cost is of great importance. The first point to note in this connexion is that the market price of any given article of food is no true indication of cheapness or dearness, for the market price of a food is regulated by such considerations as flavour and rarity and not by its nutritive value. The true cost of a food can only be estimated by calculating how much tissue- and energy-forming material it yields in return for a given sum expended upon it. The following table shows the amount of tissue-forming material (proteid) and energy (expressed in calories) which can be obtained for the sum of one shilling expended on some typical articles of food:—

	Proteid (Grms.).	Energy (Calories).
Bread . . .	283	10,764
Peas	572	8,921
Potatoes . . .	54	3,796
Milk	114	3,000
Butter . . .	3·5	2,884
Apples . . .	27	2,856
Cheese . . .	272·5	2,638
Cod	218	953
Eggs	79	839
Lean Beef . . .	127	829

It will be seen that the vegetable foods are, as a class, much cheaper than the animal foods, whether one regards them as sources of proteid or of energy. Of the nutritive constituents of foods carbohydrates are by far the cheapest, mainly because they are of purely vegetable origin. Sugar, indeed, is the cheapest source of energy known. Fat, on the other hand, is an expensive constituent, chiefly for the reason that the fatty constituents of the dietary, in this country at least, are mainly derived from animal foods. The cheapest sources of proteid, it is worth remembering, are skimmed milk, some forms of fish (*e.g.* herrings and salt fish), cheese, the inferior cuts of meat, and, for those who can digest them, the pulses; whilst the most economical forms of fat are margarine and dripping, and—again for those who can digest them—nuts. When

it is remembered that of the wages received by a working man fully 50 per cent must be spent on food alone, the importance of a knowledge of these estimates will be obvious.

From what has been said it will be evident that it is no easy matter to pronounce an opinion upon the relative value of different foods or different diets offhand. Consideration must be directed not only to their chemical composition, but also to their behaviour in the stomach and intestine and their true relative cost. The *best* food or diet, however, will always be that which is richest as a source of proteid and energy, is easily digested in the stomach and well absorbed by the intestine, and yields these advantages at the smallest cost. Unfortunately there is no one food which is pre-eminent in all these respects, and for that reason the adoption of a mixed diet must always best meet the requirements of healthy nutrition.

3. The Amount of Food required in Health

The question as to how much food is required to maintain the body in a state of health resolves itself into two separate problems: (1) How much proteid is required daily for the repair of the tissues? and (2) What amount of potential energy must be supplied in order to meet the outgoings in the form of heat and work? We shall consider these problems separately.

1. Physiologists are not yet agreed as to the *minimum amount of proteid which the body requires daily* in order to keep the tissues in full repair. The question at issue is really this: Should we make use of proteid merely as a tissue-repairer, or should we employ it partly as a source of energy as well? Voit long ago stated that 118 grammes of proteid was the minimum amount for any satisfactory diet. More recent observations, however, have shown conclusively that nitrogenous equilibrium can be maintained on much lower quantities than that—even upon 75 grammes or less.[1] But it does not necessarily follow that it is advisable to live upon a proteid minimum, even though it entails no loss of body substance; for to do so means but a small reserve of circulating proteid, in certain circumstances, which may conceivably be a disadvantage. In addition to this there is reason to believe that proteid acts as a stimulant to the cells, and therefore to the body as a whole, and that a minimum consumption of it may lessen energy and the powers of resistance, besides lowering the rate at which muscular and

[1] Since the above was written, an account of some elaborate experiments has been published by Chittenden (*Physiological Economy in Nutrition.* New York, Frederick A. Stokes Company, 1904), which show that health and efficiency can be maintained for a period of several months on a daily consumption of proteid which is less than half of that given in the usual standards, and without any corresponding increase in the total energy-value of the diet, and this is the case even though a considerable amount of muscular work is being performed. Further experience is needed before it is proved that his results are true for an indefinite period of time; but should this be done, the conclusion is inevitable that the usual dietary standards are too high, and involve a needless expenditure of physiological energy.

nervous work can be performed. The problem is further complicated by the fact that the amount of proteid upon which nitrogenous equilibrium can be maintained depends largely upon the nature and amount of the other constituents of the diet. For instance, if a large amount of carbohydrate is consumed, it is possible to maintain the nitrogenous tissues upon a comparatively small intake of proteid, for the carbohydrates are very efficient "proteid sparers," shielding them from destruction in the production of energy, and leaving them free to perform the more important duty of maintaining the tissues in a state of repair. Hence it is that there is not necessarily any loss of nitrogen from the body when fed on a large amount of purely vegetable food, for although such a diet is apt to be poor in proteid, it is yet so rich in carbohydrates that what proteid it does contain can be entirely devoted to the upkeep of the nitrogenous tissues. There is thus, strictly speaking, no one proteid minimum, for each diet will have its own proteid minimum depending upon the amount of "proteid sparers" which it contains. Meanwhile, and until a final solution of the problem, if that indeed be possible, has been arrived at, most authors have agreed to accept 120 grammes as the standard amount of proteid required daily by an average man doing a moderate amount of muscular work.

2. The question, *How much potential energy must be supplied daily in the food?* is one to which it is much easier to give a satisfactory reply. Both experiment in the laboratory and observation of the freely chosen diets of healthy persons agree in showing that an amount of energy equivalent to 3500 calories is required daily by a man of average weight who is performing a moderate amount of physical labour. What proportion of this total should be contributed by each nutritive constituent of the food is, so far at least as the tissues are concerned, largely a matter of indifference. As has already been shown, it is impossible to say definitely whether any of it should be derived from proteid at all, and whether to use proteid as a source of energy may not really be described as a "*luxus* consumption" of it. Most authors are agreed, however, that not more than 15 per cent of the total calories yielded by the diet should be derived from proteid. How much of the remainder should be derived from carbohydrates and how much from fat is partly a digestive and partly an economic question. The work of the digestive organs is certainly easier when both fat and carbohydrates are made use of in moderate amount. Perhaps one may say that on an average the diet should contain about 60 grammes of fat and 500 of carbohydrate. Those to whom expense is an object, however, will in all probability instinctively adopt a higher proportion of such a cheap constituent as the carbohydrates and a smaller amount of fat. Opportunity also is a determining factor. The Esquimaux, for example, make a large use of fat, because they are unable to obtain a sufficiency of carbohydrates; and, conversely, the natives of warm climates derive the greater proportion of their energy from rice or other starchy foods, as in the latitudes in which they live these are abundant. In this, as in so many

other dietetic questions, necessity decides what must be eaten, and custom makes it the most agreeable and, it may be added, the most digestible.

4. Influence of Various Conditions upon the Amount of Food required

The standard diet above described, which contains 120 grammes of proteid and yields about 3000 or 3500 calories of energy, is that which is suitable for a man of average weight doing a moderate amount of muscular work. Attention will now be directed to the modifications which must be made in this standard to meet variations in physical conditions and modes of life.

1. *Influence of Work and Rest.*—The amount of muscular work performed influences the quantity of food required more than any other factor. The following estimates have been made of the amount of energy which must be supplied for different forms of work :—

1. Sedentary work . . .	2500 calories.
2. Professional work . . .	2500 to 3000 calories.
3. Moderate muscular work . .	3000 to 3500 calories.
4. Severe muscular work . .	3500 to 4000 calories.
5. Hard labour . . .	5000 calories.

It seems to be a matter of indifference in what form the increased energy requisite for muscular work is supplied, though there is some reason to suppose that where rapidity of output is essential proteid is more suitable than carbohydrates or fats. In any case a higher proportion of proteid than usual must be supplied in order to cover the increased wear and tear of tissue which muscular work involves. Persons who are completely at rest, and particularly if their loss of heat is minimised at the same time, as, for example, in the case of patients in bed, require a much smaller supply of food than the standard fixed for health, and may maintain weight on a daily intake of 2000 calories or even less.

As regards the relation of diet to mental labour we know almost nothing, but there is no clear evidence to show that brain-work demands either an increase in the total amount of food or a greater relative supply of any one nutritive constituent. In such circumstances the digestibility of the food appears to be of more importance than its amount (Atwater).

2. *Influence of Sex and Age.*—Other things being equal, a woman requires less food than a man, mainly owing to the lesser bulk of the muscles. A child, on the other hand, has a relatively greater demand for food than the adult, partly because he is actively growing, and partly because of his comparatively large body surface, which induces great loss of heat. The following standards are of at least approximate accuracy in this relation :—

A child under 2	requires	0·3	the food of a man at moderate muscular work.		
,, of 3 to 5	,,	0·4	,,	,,	,,
,, 6 to 9	,,	0·5	,,	,,	,,
,, 10 to 13	,,	0·6	,,	,,	,,
A girl of 14 to 16	,,	0·7	,,	,,	,,
A boy of 14 to 16	,,	0·8	,,	,,	,,
A woman	,,	0·8	,,	,,	,,

The dietetic requirements of old age are just the reverse of those of childhood; for the assimilative and digestive powers being on the wane, and the bodily activities restricted, less food is required. Hence the diet of old people should be rather spare (*vide* p. 204).

3. *Influence of Weight and Build.*—The greater the weight of living tissue to be maintained the greater the amount of food required. All tissues, however, are not for practical purposes equally alive. Fat and bone, for example, require but little maintenance; muscle a great deal. Hence a man whose weight is due chiefly to large muscular development will require a more liberal diet than one whose weight is the result of an accumulation of fat. In the case of a man of average muscular power one may state the amount of energy which must be supplied daily per unit of weight thus:—

Condition.	Calories per kilo of body weight.
In bed	30 to 34
At rest, but not in bed . . .	34 ,, 40
Moderate muscular work . . .	40 ,, 45
Hard ,, ,, . . .	45 ,, 60

It has also been calculated that very fat people require only 26 to 36 calories per kilo of weight, whilst for under-nourished and cachectic persons about 25 will suffice.

The *shape* of the body is also of importance in determining the amount of food required, for the greater the body surface relative to its bulk the greater is the amount of energy which must be supplied to make good the increased loss of heat. Thus tall, thin persons, having a relatively large surface, require a greater amount of food than those who are short and stout. Recognition of the influence which the extent of body surface exerts on the amount of food required will prevent one from being puzzled by the apparent anomaly that the stoutness or leanness of an individual has often very little to do with the amount he eats.

4. *Influence of Climate and Season.*—Climate and season exert comparatively little influence upon the amount of food required, for the temperature of the body is regulated more by varying the amount of heat loss than by increasing or diminishing heat production. Extreme cold, however, seems to be better borne if there is an increased consumption of food, preferably of fatty articles; whilst in hot weather or in warm climates it is probably advisable to restrict the total intake somewhat, and especially, perhaps, the amount of proteid.

5. *Influence of Personal Peculiarity.*—Of the influence of idiosyncrasy on the amount of food required nothing definite is known. Common observation, indeed, would appear to show that some people are able to thrive upon less food than others, but such differences can be largely explained by differences in build and weight, the importance of which has already been considered. It must not be forgotten, too, that the more "energetic" a person is—that is to say, the more numerous and rapid his muscular movements—the greater will be the amount of food which he requires, and there is nothing in which individuals differ more than in the amount of energy they display. Allowing for all this, there is still room for the belief that some people are more economical machines than others, and make a better use of the food they consume—perhaps expending less of it in heat production, This belief, however, still lacks the support of any accurate scientific observations.

5. Effects of Over- and Under-Feeding

The effects of habitual over-feeding depend upon whether the excessive consumption is chiefly in the form of proteid or mainly in that of carbohydrates and fats. Proteid can hardly be stored up in the body, and when consumed in excess the products of its destruction flood the circulation and have to be eliminated by the kidney. Hence may result high blood pressure, arterial degeneration, renal disease, and, in some persons at least, gout. Excess of carbohydrates or fats, on the other hand, is converted into fatty tissue, with the result of producing obesity. In considering the effects of habitual under-feeding one has again to distinguish between the results of a deficiency in the building material (proteid) of the diet and those of a reduction in the total amount of energy supplied. When the minimum amount of proteid on which life can be maintained was discussed, it was pointed out that a lack of this ingredient in the diet is believed to reduce "energy" and the power of resistance to unfavourable influences. Further, as proteid is essential to growth it will readily be understood that any deficiency of it in the diet will tell most unfavourably on the young, and result in a stunting of physique which may be irreparable.

If the diet supplies too little total energy to the body the power of producing work is impaired, and it would appear also that the general vitality is lowered, so that the body more readily becomes attacked by disease. Here, again, the worst effects are exerted upon the young, and it is during the period when growth is still taking place that the advantages of an abundant and varied diet are most apparent.

6. Characters of the Principal Food-Stuffs

1. *Animal Foods.*—The animal foods as a class are characterised by their relative richness in proteid and fat. In virtue of the former property they constitute an important source of tissue-forming material.

In addition they are compact foods, containing much nutriment in small bulk, are comparatively easy of digestion, and are very completely absorbed. It is as a supplementary source of proteid that they are chiefly of value in a mixed diet, whilst their sapid character renders them often of great value in the cuisine of the sick-room.

(*a*) *Meat.*—The flesh of animals, which constitutes meat, consists of microscopic tubes containing proteid, held together by a varying amount of connective tissue. The more abundant and fibrous the connective tissue is, the tougher the meat. Embedded in the connective tissue is a varying quantity of fat which, when abundant, may so envelop the proteid-containing tubes as to interfere with the access to them of the digestive juices, and so lessen their digestibility. In addition to proteids, connective tissue, and fat, meat contains a considerable quantity of mineral matter, chiefly in the form of salts of potash and phosphoric acid. The flavour of meat is due to the presence of "extractives," nitrogenous bodies of complex constitution which help in calling out a flow of gastric juice, but are of no direct nutritive value.

The following table represents the chemical composition of some of the chief varieties of meat cut from the cold roast joint as commonly eaten (Tankard):—

	Water.	Proteid.	Fat.	Mineral Matter.
Mutton	39·76	29·04	26·80	1·93
Lamb	59·89	24·69	11·95	1·63
Beef	45·63	26·50	24·21	1·21
Veal	51·88	32·19	11·39	1·57
Pork	44·90	32·63	19·67	1·86
Duck	64·13	27·12	6·06	2·04
Fowl	67·40	24·26	6·68	1·37

The digestion of meat takes place chiefly in the stomach, the rate of the process largely depending on the method of cooking. It has been found, for instance, that 3½ ounces of meat (a small helping) disappear completely from the stomach in the following times:—

Raw	2 hours.
Half boiled	2½ "
Wholly boiled	3 "
Half roasted	3 "
Wholly roasted	4 "

Raw or underdone meat is therefore more suitable for persons of weak digestion than that which has been fully cooked.

The *breast* of chicken or game is perhaps the most digestible form of meat; mutton is more easily digested than beef, and beef than veal. Pork, because of the amount of fat which it contains, is rather difficult of digestion, and the same is true of duck and goose.

The composition of some of the viscera of animals which are commonly eaten as food is as follows :—

	Water.	Proteid.	Fat.	Carbohydrates.	Mineral Matter.
Kidney . . .	78·7	16·8	3·2	...	1·3
Liver . . .	71·2	20·7	4·5	1·5	1·6
Heart . . .	69·5	17·0	12·6	...	0·9
Lung . . .	75·9	20·2	2·8	...	1·2
Sweetbread . .	70·9	16·8	12·1	...	1·6
Tripe . . .	74·6	16·4	8·5	...	0·5
Tongue (fresh) . .	63·8	17·1	18·1	..	1·0
Brain . . .	80·6	8·8	9·3	...	1·1

Of these, sweetbreads and tripe are the most digestible, and are of high nutritive value, though the amount of nucleins which the former contain render them unsuitable for the gouty. Brains, though easy of digestion in the stomach, are very imperfectly absorbed.

(*b*) *Fish* resembles meat in its general structure and composition, but contains, as a rule, a higher proportion of water and less proteid. According to the amount of fat which they contain, fish may be placed in the following groups :—

1. More than 5 per cent of fat :—
   Eel (18 per cent), salmon (12 per cent), turbot (12 per cent), herring (8 per cent).
2. From 2 to 8 per cent of fat :—
   Halibut (2 up to even 10 per cent), mackerel (2 to 9 per cent), Mullet (about $2\frac{1}{2}$ per cent).
3. Less than 2 per cent of fat :—
   Haddock, whiting, cod.

Haddock and whiting appear to be somewhat more easily digested than beef; but the fat fishes are rather indigestible, and should be avoided by dyspeptics. In nutritive value the fatter forms of fish are fully equal to moderately fat meat, but the lean fish, owing to their containing less proteid and more water, are considerably inferior to it. It may be reckoned that one pound and a half of cod or other white fish is only equal in nutritive value to one pound of lean beef. On the other hand, it must be remembered that, on account of their cheapness, some of the commoner varieties of fat fish, such as herring and mackerel, are amongst the most economical sources of animal nutriment.

In the dietetics of disease white fish is sometimes ordered for the sake of its high degree of digestibility, and in renal disease it is believed to be less injurious than meat. The evidence for this belief, however, rests upon rather slender foundations.

Oysters may be conveniently considered with fish. Chemically they

contain representatives of all three nutritive constituents, the following being their average composition :—

Water	88·3	per cent.
Nitrogenous substances	6·1	„
Fat	1·4	„
Carbohydrates (glycogen)	3·3	„
Salts	1·9	„

Though very easily digested in the raw state, their nutritive value is not high, three dozen of moderate size containing at most but five ounces of nutriment. The presence of glycogen in them renders them an unsuitable food for diabetics in whom a strict diet is being enforced.

(*c*) *Eggs* are valuable sources of proteid and fat. The following represents the average composition of the white and yolk respectively :—

	White.	Yolk.
Water	86·61	47·53
Proteid	10·93	17·45
Fat	0·14	33·32
Mineral matter	0·71	1·67

The yolk contains a relatively large amount of lecithin and other compounds of phosphorus, as well as an organic compound of iron, in virtue of which peculiarities it is a specially valuable food for growing tissues and for the nervous system. The digestibility of eggs varies greatly with the form in which they are eaten. Raw or lightly boiled or poached eggs are more rapidly disposed of by the stomach than those which have been thoroughly boiled. Raw or lightly cooked eggs indeed must rank amongst the most digestible of all foods. Eggs leave a very small residue in the intestine, and this, coupled with their richness in lime, probably explains the constipating effect which they produce in many persons. In the diet of the invalid they are chiefly of value as a compact and easily digested form of proteid and fat, and for the ease with which they lend themselves to the manipulations of the cook.

(*d*) *Milk and its Derivatives.*—Milk is one of the few complete foods which we possess, for it contains in itself representatives of all the nutritive constituents. An average sample of cow's milk yields about $12\frac{1}{2}$ per cent of solid matter, which is made up of 3·3 per cent of proteid, 3·6 per cent of fat, 4 to $4\frac{1}{2}$ per cent of sugar, and 0·73 per cent of mineral matter. The proteid is chiefly in the form of casein, the remainder being lactalbumin. The casein is kept in a state of imperfect solution by its union with salts of lime; if separated from these by the addition of acid, it is thrown down in the form of a flocculent precipitate. This happens when milk curdles. The fat of milk is present in the form of a very fine emulsion. It contains a relatively large proportion of olein, and has therefore a low melting-point. It is to this, and to its minute state of division, that milk fat owes its high degree of digestibility. The sugar of milk, lactose, is characterised by a comparative

absence of sweetness and by its inability to undergo fermentation by yeast. Both of these characteristics enhance its value as a food, particularly in cases of dyspepsia. The mineral matters found in milk consist mainly of salts of calcium and phosphoric acid. In virtue of this, milk is one of the best dietetic sources of lime salts that we possess. As it is clotted by rennin in the stomach, milk is not so easy of digestion as one might expect, the density of the clot being in some cases a serious obstacle to its solution by the gastric juice. By diluting the milk with water, or, even better, with a mucilaginous decoction, such as barley water, by precipitating the lime salts by the addition of citrate of soda, or by previously peptonising it, the density of the clot can be greatly diminished or its formation avoided altogether, and the digestibility of the milk increased in proportion. These methods are frequently employed in the feeding of the sick. Boiling diminishes somewhat the digestibility of milk, but not to any great extent. Milk is not very completely absorbed in the intestine; in this respect, indeed, it compares unfavourably with most other animal foods. The constipating effect which it undoubtedly exerts in some people is, therefore, rather to be attributed to the amount of lime which it contains than to its leaving a small residue in the intestine. It is an interesting fact that young children seem to absorb milk more easily than adults. Although it contains representatives of all the nutritive constituents, milk is too bulky to be regarded as a perfect food, as about 8 pints of it would be required daily to supply the amount of energy required by a man doing a moderate amount of muscular work; on the other hand, it is a cheap source of proteid, whilst its fluid form, and the ease with which it is digested, give it a unique value as a food for the sick. Milk seems to exert a restraining influence on intestinal putrefaction, probably owing to the production of lactic acid by a splitting up of the milk-sugar. It is to this property that it owes many of its advantages as a food in intestinal disorders.

Whey is the fluid which is left after the casein has been removed from milk. It contains all the original sugar and most of the mineral ingredients of the milk, but only about 0·8 per cent of proteid and traces of fat. It is not of high nutritive value, but is a useful temporary food in some cases of illness, and possesses in addition slight laxative and diuretic properties

Cream consists essentially of milk fat along with traces of proteid and sugar. The exact proportion of fat which it contains varies greatly in different samples, but about 45 per cent is usually found in ordinary centrifugal cream. As milk fat is very easily digested, cream must be regarded as a valuable means of adding fat to the diet, in cases in which such an addition is desirable. Butter resembles cream in its general properties, but contains about twice as much fat. Margarine, derived from meat fats, which is an artificial substitute for butter, resembles butter very closely in its chemical composition, and, in digestibility and capability of absorption, is practically identical with it.

Koumiss and *Kephir* are derivatives of milk which are sometimes made use of in feeding the sick. They are fermented beverages, derived from mare's milk and cow's milk respectively by acting upon them by a ferment consisting of lactic-acid-forming organisms and yeasts. The sugar of the milk under this process is in part converted into lactic acid, in part broken up into alcohol and carbonic acid, whilst the casein is thrown down by the acid in a finely flocculent form. An average sample of kephir will contain about 1·5 per cent of sugar, 2 per cent of fat, 0·8 per cent of lactic acid, and 2 per cent of alcohol, besides all the original proteid of the milk. The great advantage of these beverages is their high degree of digestibility, in virtue of which enormous quantities of them may be given without detriment. They have been largely used as a means of carrying out forced feeding in pulmonary tuberculosis and other wasting diseases.

Cheese consists of the casein and fat of milk, of each of which it contains usually about 30 per cent, the remainder being waste. Its thorough infiltration with fat and the difficulty of chewing it properly render cheese slow of digestion in the stomach. On the other hand, it is very completely absorbed in the intestine, and is of high nutritive value for those who can digest it. It is useful in the feeding of diabetics.

2. *The Vegetable Foods* differ from the animal foods as a class in containing much carbohydrate and relatively little proteid and fat. This, however, is not true of all vegetable foods: nuts, for example, are rich in fat, and the pulses are rich in proteid; but, as a general rule, the statement holds good. Structurally, the most striking peculiarity of the vegetable foods is the presence in them of a framework of cellulose. Various important consequences follow from this. In the first place, the cellulose framework causes many vegetable foods to be very bulky; in the second place, by enclosing the nutritive constituents in an impermeable envelope, it renders them difficult of digestion and absorption; and, in the third place, by the production of marsh-gas in the intestine many vegetable foods are apt to give rise to flatulence. It is thus clear that the vegetable foods, unless suitably prepared, are apt to tax the powers of the stomach and intestine much more than the animal foods. As a general rule, therefore, they are not well borne in cases of dyspepsia.

As far as nutritive value is concerned, it is chiefly in respect of proteid that the vegetable foods are apt to be lacking. This is due not only to the initial poverty in that ingredient, which characterises most of them, but also because such proteid as they do contain is apt, for the reasons already given, to be but badly absorbed.

Vegetarianism, therefore, tends, unless a very large bulk of food can be digested, to result in a deficient supply of proteid to the blood with all the consequences which that entails.

The vegetable foods may be considered in the following groups:—

(*a*) *The Cereals*.—The following table shows the composition of some of the commoner food products derived from cereals:—

	Water.	Proteid.	Fat.	Carbo-hydrates.	Fibre.	Mineral Matter.
Wheat Meal	12·1	12·9	1·9	70·3	1·6	1·2
Fine Wheat Flour	13·0	9·5	0·8	75·3	0·7	0·7
Oatmeal	7·2	14·2	7·3	65·9	3·5	1·9
Barley Meal	11·9	10·0	2·2	71·5	1·8	2·6
Pearl Barley	12·7	7·4	1·2	76·7	0·8	1·2
Fine Rye Flour	11·2	6·7	0·9	80·0	0·8	0·4
Maize Meal	11·4	8·5	4·6	72·8	1·4	1·3
Rice	12·4	6·9	0·4	79·4	0·4	0·5

It will be observed that starch predominates in them all, and that, with the exception of oats and maize, they are very poor in fat.

Wheat is the staple cereal in use in this country, and is chiefly consumed in the form of *bread*. The average composition of bread prepared from white flour and from whole wheat meal is as follows:—

	White Bread.	Whole-Meal Bread.
Water	40·0	45·0
Proteid	6·5	6·3
Fat	1·0	1·2
Starch, etc.	51·2	44·8
Cellulose	0·3	1·5
Ash	1·0	1·2

It will be noticed that, owing to the greater amount of moisture which it contains, whole-meal bread is not appreciably richer in any of the nutritive constituents than white. On the other hand, digestive experiments show that the absorption of whole-meal bread in the intestine is considerably inferior to that of white bread, so that the supposed superiority of the former as a source of nutriment is really based upon a fallacy.

"Germ" breads (such as Hovis) contain the embryo of the wheat, and are therefore somewhat richer in proteid and fat than white bread. In "malted" breads (*e.g.* Bermaline) part of the starch has been converted into soluble forms (dextrins and maltose). As, however, the proportion of starch so changed is never more than 10 per cent, the digestibility of malted bread is not greatly superior to that of good white bread.

The effect of toasting bread is to drive off most of its moisture, and to rupture some of the starch grains, while part of the starch is converted into dextrins and caramel.

(*b*) *The Pulses* include peas, beans, and lentils. They are the richest in proteid of all the vegetable foods, containing in their dried form 20 to 25 per cent of it. They are rich also in mineral matter, chiefly salts of lime, but are poor in fat. Most of the pulses contain a bitter principle, which makes them distasteful to many persons, and their richness in sulphur renders them peculiarly apt to produce flatulence. The soy

bean, which belongs to this group, contains abundance of proteid and fat, but is poor in starch; for this reason it is sometimes used in the preparation of bread for diabetics. The patent preparation known as Revalenta Arabica consists mainly of lentil flour.

(*c*) *The Roots and Tubers* contain much starch, but very little proteid. They owe part of their value as foods to the abundance of potash salts present in their ash. The following table shows the composition of some of the chief members of the group:—

COMPOSITION OF ROOTS AND TUBERS.

	Water.	Proteid.	Carbo-hydrates.	Fat.	Fibre.	Mineral Matter.	Extrac-tives.
Potatoes	76·7	1·2	19·1	0·1	0·6	0·9	1·4
Carrots	85·7	0·5	10·1	0·3	1·5	0·9	1·0
Turnips	90·3	0·9	5·0	0·1	1·8	0·8	1·1
Radishes	90·8	1·4	4·6	0·1	...	0·7	
Beetroots	83·9	0·5	11·0	0·1	3·0	0·9	1·0
Parsnips	80·1	1·4	14·1	1·0	2·1	1·3	
Artichokes	79·8	2·3	14·5	0·3	2·0	1·0	
Onions	89·1	1·6	6·3	0·3	2·0	0·6	

It is worth noting that potatoes contain less than half as much starch as bread, and are therefore less unsuitable as a food for diabetics than bread. Tapioca, sago, and arrowroot are practically pure forms of starch.

(*d*) *Green Vegetables* contain a great deal of water, almost no nitrogenous matter or fat, and only a small quantity of carbohydrates (2 to 8 per cent). They are specially rich in cellulose, which, along with the amount of water they contain, renders them bulky foods and incapable of anything approaching complete absorption. Like the tubers they are valuable sources of potash salts, whilst their bulkiness renders them useful additions to the diet in some forms of constipation.

(*e*) *Fruits.*—The approximate composition of the fresh fruits is as follows:—

Water	85 to 90 per cent.
Proteid	0·5 „
Fat	0·5 „
Carbohydrates	$5\frac{1}{2}$ to $10\frac{1}{2}$ „
Cellulose	$2\frac{1}{2}$ „
Mineral matters	0·5 „

Of the carbohydrates present about half consist of sugar (lævulose). As fruit sugar is more easily assimilated in diabetes than any other form, it is often safe to allow sufferers from that disease to consume small quantities of fresh fruit. The mineral constituents of fruits consist chiefly of vegetable salts of potash, whilst their flavour is due to the presence of small quantities of ethereal oils.

Nuts differ from the fresh fruits in being of high nutritive value; this they owe to their richness in fat. Their general composition is as follows:—

Water	4 to 5 per cent.
Proteid	15 to 20 "
Fat	50 to 60 "
Carbohydrates . . .	9 to 12 "
Cellulose	3 to 5 "
Mineral matter . . .	1 "

The dense cellulose framework which nuts contain renders them difficult of digestion in the stomach unless they have been previously ground. We have no information as to the extent to which they can be absorbed.

Mushrooms and other edible *fungi* consist chiefly of water and cellulose; being also difficult of digestion and badly absorbed, their nutritive value is extremely low. Iceland and Irish moss, too, are substances which are practically devoid of any real nutritive qualities.

7. The Mineral Constituents of Food

The chief mineral matters present in food are salts of calcium, magnesium, iron, sodium, and potassium, along with phosphorus, chlorine, sulphur, and traces of silica, fluorine, and iodine. We know that most, if not all, of these are necessary to aid in the formation and upkeep of the tissues, but of the exact amount of each which must be supplied daily we know nothing. There is little fear, however, of a lack of mineral constituents; an ordinary mixed diet, provided it be sufficient in other respects, is sure to contain an ample quantity of mineral ingredients to meet the demands of the body.

The foods richest in *calcium*, which is so important in the formation of bone, are milk and eggs amongst animal foods, and the cereals, pulses, and some green vegetables amongst vegetable foods. On the other hand, meat, fish, fruits, and potatoes are poor in calcium, and it has even been suggested that patients who have a tendency to calcification of the arteries should confine their diet to these articles.

Iron is contained in greatest abundance in yolk of egg, the red meats, oatmeal, Egyptian lentils, and spinach. Milk contains very little iron; this may help to explain the tendency of an exclusively milk diet to result in the production of anæmia.

Sodium is chiefly consumed as common salt. In this form it is taken as a condiment rather than a food, but there is no trustworthy evidence to show that its use in that form is in any way harmful, whereas it certainly seems to aid digestion in some persons.

Potash is contained abundantly in meat and in many vegetable foods. The vegetable salts of potash seem to be of special value in helping to maintain a proper degree of alkalinity in the blood.

Phosphorus is a mineral constituent essential for the formation of growing tissues. It enters into the composition of all cell-nuclei, and is abundantly present in the central nervous system and bones. In the food it is found in both organic and inorganic combinations. There is some reason to believe that its organic compounds are more useful for purposes of nutrition than the inorganic phosphates. The foods richest in organic compounds of phosphorus are yolk of egg, thymus, fish-roe, calves' brains, and the germ of wheat.

Oxalic Acid is usually present in the diet in an inorganic form combined with calcium. Tea, rhubarb, and spinach contain more oxalate of lime than any other foods. Tomatoes contain very little in spite of an impression to the contrary. Animal foods are almost free from oxalates.

8. Beverages

1. *Water and Mineral Waters.*—In ordinary circumstances about two and one-third pints of water must be supplied in the liquid form daily in order to make good the excretion of it by the kidneys, skin, and lungs. It is obvious, however, that the exact quantity required must vary within very wide limits, chiefly dependent upon the activity of the skin. The drinking of large quantities of water certainly "washes out" the blood and tissues and removes from the body waste nitrogenous matters. At the same time the temporary increase in the volume of the blood throws an increased amount of work upon the heart. If the consumption of water be restricted the volume of the blood is temporarily lessened, but the deficit is speedily made good by absorption from the tissues, which consequently become drier. A dry diet is thus of use in promoting the absorption of fluid from the tissues in cases of dropsy. There is no proof that the free drinking of water with meals retards digestion in health, but it seems to favour the production of flatulence in atonic conditions of the stomach. Water is not absorbed from the gastric mucous membrane, and consequently when there is pyloric stenosis it accumulates in the stomach, helping to bring about dilatation of that organ, whilst the tissues become dry. For this reason it is often advisable to supply water in the form of copious enemas in such cases.

Mineral Waters consist of water impregnated with carbonic acid gas, and sometimes contain some mineral matter in solution as well, usually bicarbonate of soda and salts of lime. Their action depends chiefly upon the carbonic acid they contain, which acts as a stimulant to digestion. Their use should be avoided in atonic conditions of the stomach in which there is a tendency to the production of flatulence.

2. *Tea, Coffee, and Cocoa* are sometimes spoken of collectively as the alkaloidal beverages, because their action depends in the case of the two former upon caffeine, and in that of the latter on theobromine. In addition to caffeine, *tea* contains tannic acid and a volatile oil. A teacupful of tea prepared in the ordinary way contains about 1 grain of caffeine and 2 or 3 grains of tannic acid. China tea contains less tannic

acid than the other sorts, and the beverage which has been infused for a short time much less than that which is the result of more prolonged extraction. Tannic acid interferes seriously with gastric digestion, and for that reason China tea, lightly infused, is the most suitable form for use in dyspepsia. A teacupful of black *coffee* of the strength of 2 ounces to the pint contains just about as much caffeine and tannic acid as an equal quantity of tea. In addition it contains some of the volatile oil, caffeol, which is developed in the process of roasting. Coffee is frequently adulterated with chicory, the roasted root of the wild endive, which contains a considerable proportion of caramel. Its use is in no way injurious to health, but it is, of course, devoid of the special physiological properties of coffee. Neither tea nor coffee is in any sense a food, but they exert stimulating effects on the nervous system, and to some extent also on the heart, in virtue of the caffeine which they contain. Both lessen the feeling of fatigue, and seem to accelerate and facilitate brain action. Their use should be avoided by patients who suffer from nervousness or insomnia.

The active principle of *cocoa* is theobromine, of which, however, it contains only a small amount. Pure cocoa powder contains in addition about 30 per cent of fat and a certain amount of starch. Cocoa contains too little alkaloid to exert any real stimulating effect on the brain, and in spite of its comparative richness in fat it has no claim to be a food, as so little of it can be taken at a time. *Chocolate*, on the other hand, is rich both in fat and sugar, and must be regarded as a nutritious and valuable food for those who are capable of digesting it in considerable quantities.

3. *Alcoholic Beverages.*—The effects of these beverages in health and disease depend upon the amount of ethyl-alcohol which they contain. The physiological action of alcohol, though still to some extent the subject of dispute, may be summed up as follows :—(*a*) Locally, and in strong solution, it acts as a tissue irritant. Hence the tendency of neat spirits to produce pharyngitis and gastritis. (*b*) In the stomach, unless present in large amount, it aids rather than retards digestion. This effect is due both to its causing an increased secretion of gastric juice and to its stimulating the muscular movements of the stomach wall. (*c*) It increases the frequency, and to some extent also the force, of the heart, especially in concentrated doses; but these effects are of short duration. It also tends to dilate the peripheral blood-vessels. (*d*) In large (intoxicating) doses it tends to reduce the body temperature. (*e*) It acts as a depressant to the metabolic activity of the cells and lessens the power of doing muscular work. (*f*) It is completely oxidised in the body, one gramme yielding in the process seven calories of heat, and in so doing spares body fat from combustion, and to some extent proteid also. It is thus in one sense entitled to be regarded as a food, but its nutritive properties are entirely overshadowed by its actions as a drug. (*g*) It acts as a temporary cerebral stimulant, but this effect is probably to be attributed rather to paralysis of inhibitory centres

and to increased activity of the cerebral circulation than to any direct stimulation of the cells of the brain. (*h*) Like most drugs its effects are largely influenced by personal factors, in consequence of which it may be taken in moderate quantity by some persons without demonstrable harm, but is to others a slow poison.

Alcohol is usually consumed in the form of spirits, beer, or wine. Spirits (brandy, whisky, rum) contain about 45 per cent of alcohol by volume; beers, 4 to 7 per cent; natural wines (claret, hock, Italian wines), 10 per cent; and fortified wines (port and sherry), 20 to 25 per cent. Champagne, which is slightly fortified, contains from 10 to 15 per cent of alcohol. The action of all of these depends mainly upon the proportion of alcohol which they contain, but some of them contain other ingredients which also play a part. Thus in the case of spirits and the fortified wines, some of the action upon the nervous system is to be ascribed to the presence of small quantities of ethers, and these seem to be particularly valuable in some forms of disease. The large amount of tartaric acid present in some wines is also not without influence upon their physiological action, whilst the presence of sugar and dextrin in the malt liquors, in quantities amounting to from 3 to 5 per cent, confers upon them a not inconsiderable nutritive value. It is usually stated that from 1 to $1\frac{1}{2}$ fluid ounces of absolute alcohol is the amount which can be completely oxidised in the body in one day. This would be contained in one glass of spirits, two and a half glasses of one of the stronger wines, one tumblerful of any natural wine, or one imperial pint of bottled beer. These quantities, however, are by no means absolute; for there can be no doubt that the power of oxidising alcohol varies greatly in different persons, and in the same person under different conditions.

9. The Patent and Proprietary Foods

It will be convenient to consider these under the following heads:—

1. *Meat Extracts.*—The following is the average composition of meat extracts:—

Water	16 to 21 per cent.
Mineral matter	18 to 22 ,,
Extractives	56 to 60 ,,

They contain also a small amount of soluble proteid and gelatin. Their most important constituents are the "extractives," complex nitrogenous substances mainly derived from the breaking down of proteid. These are of no nutritive value, and the only physiological property which they possess is the power of stimulating the secretion of gastric juice. Meat extracts are thus chiefly of use for increasing appetite and imparting flavour to other foods. They are not capable in themselves of supplying

nourishment to the body. This is true even of those which contain added beef fibre, for the amount of the latter which they contain is negligible from a dietetic standpoint.

2. *Meat Juices* are prepared by expression of the juice of the meat in the cold with subsequent evaporation *in vacuo*, with or without the addition of a preservative. The majority of them contain about 5 per cent of coagulable albumin, along with small amounts of other soluble proteids and a varying quantity of extractives and salts. Few of them contain any really large amount of proteid, and seeing that they can only be taken in very limited quantity they can never contribute appreciably to the nutrition of a patient. Those of them which contain extractives in considerable amount have the same power as the meat extracts of stimulating appetite and aiding digestion, and it is to the accomplishment of these objects that their use should be confined.

3. *Peptone Preparations.*—The foods in this group contain artificially digested proteid in varying amount. The digested proteid, though commonly spoken of as peptone, is chiefly in the form of albumoses, but this cannot be regarded as any disadvantage. Experiment has shown that the albumoses are well absorbed and are quite capable of replacing proteid in the diet, but their use in even moderate amount is apt to produce diarrhœa. For this reason the value of such preparations is limited, and in any event the occasions calling for their use are few, as it is rarely, if ever, the case that digestive power is so impaired that the natural proteids are incapable of digestion when presented in a suitable form. On the other hand, the albumoses and peptones seem, like the extractives of meat, to have the power of aiding digestion, and these preparations may sometimes be of value for that reason. Somatose is the best preparation of the class.

4. *Casein Preparations.*—This group includes such preparations as plasmon, protene, casumen, sanatogen, nutrose, and eucasin. They consist of pure casein rendered soluble by combination with an alkaline salt, usually bicarbonate of soda, and, containing as they do about two-thirds of their weight of pure proteid, must be regarded as of high nutritive value. They have the additional advantage of being soluble, odourless, colourless, and tasteless, and can therefore be easily added to other foods, and experiment has shown that they are easily digested and very completely absorbed even when taken in large amounts. Taking them all round, they are perhaps the most valuable artificial foods which have yet been invented.

5. *Malt Extracts* consist of from 60 to 70 per cent of soluble carbohydrates (chiefly maltose and dextrins) along with a small amount of nitrogenous matter; in addition, they contain the ferment diastase in an active form. They are used partly to enrich the diet with carbohydrates in an easily digested form, and partly to aid in the digestion of starch by the diastase which they contain. Virol and virvis are preparations consisting of a mixture of malt extract and marrow fat.

6. *Artificial Infant Foods* are considered elsewhere (p. 249).

10. Artificial Methods of Feeding

1. *By Nutrient Enemas.*—Experiment has shown that the substances which are best absorbed by the mucous membrane of the rectum are :—(1) peptone and albumoses; (2) eggs, with the addition of salt; (3) raw-meat juice and blood-serum; (4) dilute solutions of grape sugar or dextrin; (5) alcohol.

The best basis for the enema is peptonised milk. To eight ounces of this one may add one ounce of somatose, glucose, or dextrin, or three eggs beaten up with fifty grains of common salt. An ounce or two of red wine is sometimes a useful addition. The total bulk of the enema should not exceed nine ounces, and it should be given through an œsophageal tube of small calibre introduced as high as possible and connected with a funnel held at a height not exceeding three feet. The enema should be administered at the body temperature, the patient lying on his left side during the process, and he should remain quiet for at least an hour after the administration is completed. Not more than three enemas should be given in one day, and the lower bowel should be washed out once in the twenty-four hours during the period of rectal feeding. If ox-serum is used, three ounces may be injected every four hours, two grains of chloretone being added to each ounce, both as a preservative and as a sedative (O. F. Grünbaum).

Even when most successfully carried out, rectal feeding cannot supply a patient with more than one-third of the nutriment which he requires in a day, and although the loss of weight may be lessened by its adoption, the diminution is largely to be ascribed to the absorption of water.

Nutrient suppositories, being very imperfectly absorbed, are not to be recommended.

2. *By Subcutaneous Injection.*—In order that a food may be suitable for subcutaneous administration it must be (1) capable of direct assimilation, (2) unirritating, and (3) easily sterilised.

Few foods fulfil these requirements. Peptone cannot be directly assimilated; grape sugar is too irritating; and the natural proteids are not easily sterilised. Fat alone fulfils all three conditions, and sterilised olive oil has been injected to the extent of an ounce per day. Careful observations have shown, however, that it is so slowly absorbed into the blood that not more than twenty-five calories of heat can be furnished by it in twenty-four hours. Horse-serum, previously heated to 65° C., has been given in quantities up to four ounces, but the benefits said to be derived from it could probably be obtained almost equally well from salt solution. White of egg has also been used, but the reports as to the extent to which it can be assimilated are very conflicting. The general conclusion to which one is driven, indeed, is that, as a therapeutic measure, subcutaneous feeding is almost worthless. There is no experimental evidence as to the nutritive value of the *inunction of oil* into the skin, but in no circumstances can it be regarded as high.

R. HUTCHISON.

II. The General Principles of Dietetics in Disease; or, The Feeding of the Sick

By Sir Dyce Duckworth, M.D., LL.D., F.R.C.P.

The best writers on medicine from the earliest times have been careful to include in their treatises some account of the conduct of diseases by means of diet; and, with the advancing changes and improvement in the art of medicine, the subject of dietetics has not failed to receive an increasing share of attention.

As in respect of treatment by means of drugs or other therapeutic measures, so here we find that many changes of opinion have occurred; methods at one time in vogue have been subsequently discountenanced, and at a later date again enjoined. It must be admitted that the whole subject of dietetics has rested on an empirical basis, and been destitute of any scientific principles till within the last half of the last century. With the progress of chemistry and physiology, and by more exact clinical researches, a truly scientific basis has been laid; we have now indeed attained a measure of certainty in respect of dietetics as an instrument of medicine which may fairly be counted amongst the triumphs of modern therapeutics. This work has been done by many labourers: it has required the combined efforts of the chemist, the physiologist, and the clinical physician; and in no other manner could such a task have been accomplished.

Dietetics have always formed part of any system of medicine, however peculiar or erroneous; and contributions to the subject have come from many, and sometimes strange sources, all tending to throw light on difficult and unillumined parts of it. Of this we may feel sure when we review the claims made for their several methods by those who have enjoined high-living, low-living, "vegetarianism," hot-water drinking, total abstention from alcoholic liquids, and full stimulation with them; to say nothing of many varied and fantastic fashions in diet, all of which have been tried and fairly appraised. We have witnessed the results of so-called homœopathic treatment of patients, in which a large amount of attention is paid to diet, and feel that, in all fairness, it should be granted that at one time some accession to our knowledge of clinical dietetics came from this source.

In this article we are only concerned to set forth the general **principles and practice of dietetics**, in so far as they relate to the needs of patients suffering from various diseases; and to illustrate their application in practice. This effort necessarily comprises a due consideration of the best methods of which we have now certain knowledge, and can only be grounded upon extended and carefully weighed clinical experience.

In recent times less and less heed has been paid to drug-treatment, and more attention has been given to diet and general hygienic environ-

ment. This waning faith in drug-administration, which is unwarrantable and, to a large degree, unwise, has come of a fuller knowledge of the natural course of many morbid conditions. More reliance is placed on the *vis medicatrix naturæ*; and the art of the older drug-giving physicians has gradually fallen into desuetude, and ceased to engage the attention of many of the most capable minds in medicine. In the meantime, however, much certain knowledge has been secured—knowledge which is absolutely necessary in order to guide our efforts successfully in relieving suffering and helping on recovery.

I propose to discuss clinical dietetics under the following heads:—

General Remarks on Diet in Fevers.—A consideration of this subject naturally includes the dietetic management of the febrile state as such. The condition common to all these temporary acute illnesses is that recognised as fever or pyrexia. *Pyrexia* is a symptom which is now acknowledged by many modern observers to be no longer an inimical, but rather a friendly process so long as it is restrained within certain limits. In febrile conditions the alimentary system is more or less disturbed, almost without exception: the common indications of this are—first, the loss of natural appetite; secondly, the presence of thirst. Solid food is loathed, and if taken or pressed, commonly rejected by vomiting. The changes in the mucous surfaces tend to dryness and greatly reduced secretion from salivary and mucous glands, gastric tubular glands, duodenal (Brunner's) glands, Lieberkühn's crypts, and the pancreas. The condition of the intestinal solitary and agminate glands, when they are not specifically affected, is hardly known; nor that of the four million, more or less, villi of the intestine; but it may fairly be believed that these are in a more hyperæmic and sluggish condition, as regards normal absorptive function, than in health. Certainly, in most cases, we have clinically to note a greater or lesser degree of catarrh as pervading the entire course of the alimentary canal and of the ducts which lead into it; and in determining a diet for patients thus affected we take heed to this condition.

With respect to digestive capacity, we particularly note the absence of sufficient saliva and pancreatic secretion on the one hand, and of gastric and intestinal juices on the other; and are thus in the presence of an incapacity to deal effectually either with amylaceous food or with the several varieties of proteids. In the severer forms of prolonged fever, gastric digestion is commonly more in abeyance than that carried on in the intestines. Pyrexia thus reduces digestive capacity somewhat to that which is the normal state of the infant during the first six months of life, more particularly in respect of the inactivity of salivary and pancreatic functions.

In practice, however, it is possible to pay too much heed to these conditions, and as in politics "the King's Government must be carried on," so here our patients must be fed and sustained through the exhausting effects associated with and dependent on fever. Ample experience has proved the value of a diet consisting mainly of milk and meat juices.

The points to attend to in such a dietary relate to the purity and dilution of the milk, and to the variety and quality of the meat juices. First, with respect to milk: it is of essential importance to employ fresh milk whenever procurable. Preserved milk, in all forms, is vastly inferior for nutritive purposes. As a rule, unless the source is beyond suspicion, fresh milk is best scalded, but not boiled; it is then to be diluted with barley water, or toast and water, to the extent of one-third or one-half. If diarrhœa be present lime-water should be added, and half the amount of barley water may be thus replaced. If constipation prevail, the addition of sodium citrate or bicarbonate, instead of lime-water, to the mixed fluids is advisable—twenty or thirty grains being stirred with each pint. These measures prevent the formation of curd in any but a finely granular condition, and so prevent pain, flatulency, and intestinal disturbances. When milk is badly borne whey is often available, and to it cream may be added if desirable.

Beef juices may be given at intervals in the form of well-made beef-tea, mutton-tea, chicken or veal tea; or, occasionally, if the stomach be queasy, in the form of essences, of which there are now several trustworthy preparations. Fresh beef essences, if they can be procured, are probably better than any of the latter; and vegetable juices may be incorporated with all forms of these by immersing in the cooking-vessel a muslin bag containing finely divided vegetables such as cabbage, carrot, and so securing variety both of flavour and nutrient elements. A good rule is to change the meat juice from day to day, so as to prevent the monotony of the spoon food. Nothing better relieves such monotony than the regular administration of draughts of iced water, which are always grateful to fever patients and are too often omitted. In many cases both tea and coffee may be given with advantage. Refreshing drink is available in most febrile states—enteric fever and rheumatic fever excepted—in the form of freshly made lemonade containing a drachm of acid tartrate of potash in each pint, and a very little sugar. Regard is to be paid to the amount actually consumed, and care taken that enough is presented in each twenty-four hours. Modern skilled nursing commonly secures this, and a register is to be kept from hour to hour. Fruit is sometimes of use, and cooked apples may be given, carefully prepared, also grapes and oranges. In small-pox the latter are especially grateful. Whenever it is advisable to add to the nourishment, yolks of eggs may be added to milk or beef juice, or given with brandy as egg-flip.

We have thus considered the essentials of a so-called fever diet. The question of alcoholic fluids now presents itself. These form no routine part of dietetic treatment either in febrile or in any other morbid condition. They may, however, be necessary, and are often indispensable, in the conduct of particular cases. The skill demanded in the prescription of alcohol (that is, of alcoholised fluid of whatever kind) is of the same order as that which is required in determining the use of any other article of food or medicine for the sick. We do not affirm that because

the patient has fever, or has pneumonia, he therefore requires wine or spirit. He may or he may not. We are guided by various considerations as to the specific requirements of each patient, and we give or we withhold as the case may be. We lend ourselves to no fashion or wave of opinion in respect of food or drugs, and study the precise indications of the case for the time being. The opinions to be here stated are the result of no small experience, and have been gathered only at the bedside.

We are met at the outset by those who contend that alcohol is not a food, and has therefore no place in any dietary. We might put this opinion aside, and still contend that it has a high place in the treatment of disease. As clinicians we maintain, however, that alcohol is practically available as a food, even in the form of a pure spirit; and if the several constituents of wine be taken into consideration we have to deal with a variety of nutrient materials in subtle combination, with which alcohol, in moderate percentage, is bound up. We recognise that alcohol holds an intermediate place between carbohydrates and the fats, being less oxygenised than the former and more so than the latter. In its circulation through the system, within certain well-understood limits, it becomes destroyed and indetectible; we must therefore believe, as physiologists, that this process of destruction and transformation is attended by oxygenation and a correlative liberation of energy. We may thus explain some of the benefits derivable from the use of alcoholised fluids in various morbid states.

The *clinical indications for alcohol in febrile states* are now fairly well understood and reduced to principles. It is recognised that if no extreme pyrexia be present, if the action of the heart continue sufficiently vigorous, and food be well taken, alcohol is unnecessary. But if high fever prevails, the heart's action falters, and ordinary nutriment is taken with difficulty, at any age, and in any such case, alcohol is indicated, and its effects are under such conditions uniformly satisfactory. Thus by its use we control pyrexia, we sustain the action of the heart and the vigour of the circulation, and we secure a substitute for other nutriment till such time as a better appetite returns. We gather all these indications from the thermometer, the stethoscope, the character of the pulse, and the capacity for taking nourishment. The best form for alcoholic administration is either that of brandy or whisky well diluted with milk. Neither should be given with beef-tea or any meat juices, and the quantity is best administered at regular intervals of two or four hours, according to the particular indications. both by day and by night. The amount required is to be determined by the age and previous habits of the patient, and no less by the conditions requiring to be met. Young children bear alcohol well when it is indicated; and the amount sometimes called for may be relatively very large. In practice it is seldom necessary to exceed for an adult of average condition in any febrile state six ounces of brandy or whisky per diem, and two or three will often secure all that is needed. Over-stimulation is harmful, and is recognised by flushing,

foul breath, and discomfort. Hyperpyrexia demands the use of alcohol, and the patient is benefited by it. The cardiac indications for the use of alcohol in fever are a notable loss of tone in the first sound, especially if this be inappreciable at the base (Stokes' sign), and the associated condition of pulse that of low arterial pressure, and the phase of it known as dicrotism. The tendency to formation of sordes on the tongue or gums in grave febrile states also indicates the employment of alcohol.

Preparations of malt are certainly available in febrile conditions, and are agreeable to patients. Granulated malt extract dissolved in warm water or milk constitutes a grateful variety of readily digestible nutriment when the constant use of milky foods palls on the appetite.

When the stomach is irritable, and most of the food already indicated disagrees, recourse may be had to koumiss in small quantities (Koumiss, No. 2). Milky food may sometimes be better borne if given in doses of half an ounce to an ounce every quarter of an hour by the clock. After a few hours larger quantities may be tolerated.

The dietary thus enjoined is available for most febrile conditions, however induced, including pneumonia, all the exanthemata, and the continued fevers, with the exception of enteric fever. The same holds good for paroxysmal stages of remittent and intermittent fevers, allowance being always made for the degree of pyrexia, the age, and bodily state of each patient.

Sterilised Milk; Boiled Milk and Water; Predigested Foods.—No reference has, so far, been made to the employment of sterilised milk, or of peptonised milk and animal broths. As to the first, it is a good rule to scald all milk, unless the source and treatment of it be certainly beyond suspicion: this holds good not only in India, but all over the world. The same may be affirmed for water under all conditions, especially in India, and in the case of children and young adults.

Peptonised Foods.—With respect to peptonised food I think there is now too great a tendency to employ it. All articles of diet come best *direct from nature*, as far as possible; and without more chemical or culinary meddling than is absolutely necessary. Food is one thing, physic is another. I feel sure that peptonised foods are now too frequently administered, and are often unnecessary. They have their place, without doubt, for gastric and for rectal alimentation as a temporary measure, the object being to present predigested albumin for rapid assimilation when digestive power is at a minimum, as malted foods present predigested starches in cases where salivary and pancreatic secretions are inadequate; but it has become a fashion to resort to the use of predigested food in many cases which do not require it. Most cases of pyrexia can be treated successfully without peptonised food, but if the digestive powers be enfeebled, it may certainly be used. The liquor pancreaticus is probably one of the best agents to employ in peptonising milk, animal broth, or gruel. Nutrient enemas may be treated similarly, or predigested by the action of Taka-diastase.

Modified Diets.—It is sometimes advisable to adopt modifications of ordinary diet in the treatment of morbid conditions. Some of these are only available for temporary employment, and are known as "cures," *e.g.* milk cure, grape cure, and so forth, while others are required to meet special needs or defects arising either from disease or peculiarities of constitution.

Restriction of Water or Fluid Diet.—This is called for in several morbid conditions. In the reduction of corpulency or obesity it is of proved usefulness. Some people habitually drink too much fluid, and others too little. In treating obese patients it is found that a diminution of fluids to a limit of thirty ounces in the day adds materially to the success of any other method which may be adopted, and it is of importance that this amount should be mainly taken between and not with the meals. In some forms of chronic dyspepsia a reduction of liquids is desirable, and where there is a tendency to atony of the muscular coats of the intestinal tract, to gastrectasia and flatulence, such a course is imperative. In the treatment of aneurysms the same holds good, and this method forms an important part of that known as Tufnell's treatment, a modification of which is that now commonly adopted in such cases. In cases of cardiac dilatation, a restriction of fluids is one of the best therapeutic means at our disposal, affording marked relief to the circulation and any dropsy that may be present. Professor Von Noorden has directed attention to the value of restriction of fluids in certain conditions of nephritis, and condemns the somewhat common practice of attempting to flush the renal tubules by extra quantities of milk or water. He maintains that this proceeding is apt to strain the heart, that water is badly excreted by the kidneys when they are acutely diseased, and that a condition of hydræmia is a constant source of irritation to these organs. He believes that in many cases of contracted kidney a sensible restriction of water may save life. In severe cases of acute nephritis with reduced secretion of urine, œdema increasing and uræmia threatening, he recommends the employment of no more than half a litre (about 18 fl. oz.) of milk daily for a few days, exceptional thirst being met by a few spoonfuls of water only, and records most favourable progress under this treatment. A little cream may be added to the milk, and a small quantity of carbonate of calcium. The latter adds to the digestibility of the milk, and enables the kidneys to excrete phosphoric acid, which, when diseased, they are little able to do.

Restriction of Proteids.—It is certain that morbid conditions may be induced or maintained by the persistent employment of a diet too rich in proteids. The sufferers are commonly found amongst those who are exposed to luxury, and whose appetites are stimulated unduly by uncontrolled submission to habits and indulgences which are even now too frequently practised by those who should know better. An illustration of this is afforded generally by the well-fed meat-eating Englishman in contrast with the oatmeal- or potato-fed Scotsman or Irishman. The injurious effects of persistent over-intake of proteids are manifested

mainly by damage to the kidneys and the arterial system, and a condition of arteriosclerosis, widely spread, is one of the results of it. Chronic interstitial nephritis may be thus induced. It is certain that an excess of proteid in the diet may induce gouty conditions, or aggravate and provoke any constitutional proclivity to them. It may also provoke a state of vascular plethora, and increase the general arterial tension and the acidity of the urine.

The digestion of proteids is often better carried on than that of carbohydrate food, and this is especially the case in some forms of dyspepsia. The strain in their metabolic disposal falls with most weight probably on the liver and the kidneys. It therefore becomes of importance to restrict such articles of food as are rich in proteids in several morbid conditions, and to substitute a dietary containing less of them. In the case of persons leading a sedentary life, the amount of proteid-containing food should be reduced as a rule. Where there is a tendency to renal inadequacy and persistent high tension of the pulse, the same caution should be observed. In all forms of Bright's disease the rule holds good, but care must be taken not to reduce the nutritive value of the diet too much in the chronic parenchymatous variety, as is perhaps too commonly done. In gouty patients, while it should be the aim of the physician to maintain the best nutrition possible, it is highly important to reduce the daily intake of proteid food to a moderate limit (approximately 120 grammes). If the amount of carbohydrate food be increased in such cases, acting as a "proteid sparer," the diet may be well borne. A persistent excess of the latter, however, is sometimes responsible for the production of what is recognised as gouty obesity. It has been proved that the work of the digestive organs is rendered easier when carbohydrates and fat are added to the diet, a point which must be noted when reference is made to the so-called Salisbury method of dietary. Persistent feeding with proteids may induce hyperchlorhydria.

Restriction of Carbohydrates.—This relates to the consumption of starch and sugar, elements that enter largely into the daily food of mankind. In certain morbid conditions it is necessary to lessen the amount of these. Some dyspeptics have inadequate powers of digesting starchy food and sugar, and their di t must be altered accordingly. In health, it is found that the components of a mixed diet, which is clearly the best for man, are more fully absorbed than those of any single variety taken by itself. It is important to reduce carbohydrate food in the case of patients suffering from obesity or a tendency to it. In many cases it is found that by abstention from sugar and from starchy foods, together with a restricted intake of fluid, the extra body weight, due to fat, may be materially and rapidly lessened. In cases of saccharine diabetes or of some varieties of glycosuria it is necessary to effect a reduction, and at times a total abstention from all carbohydrate food. All such cases require careful study in regard to the inadequacy of digestive capacity for this class of food possessed by each individual. Many degrees of glycosuria are controllable by the restriction of carbohydrates to the

strict limit that can be disposed of. In the graver cases of diabetes, the glycosuria persists when total abstention from them is practised. Such a practice becomes in most instances an intolerable privation for the patient, and it is found to be a better plan to permit of some relaxation occasionally, the outlook being hopeless, and the remedy proving for the patient worse than the disease. This applies especially to younger patients in whom the prognosis is always bad. Restriction of carbohydrate is imperative in cases of glycosuria in gouty patients, and commonly affords marked benefit, and in not a few instances complete relief of the symptoms. In the fugitive glycosuria of the aged, it is unnecessary to alter the diet materially.

Forced Feeding.—Attention has been called to this method in recent years in cases of anorexia and feeble nutrition, and still more recently as a plan of treatment in cases of pulmonary tuberculosis. It is commonly associated with the name of Dr. Weir Mitchell, of Philadelphia, who introduced the method, together with enforced rest, massage, and seclusion for cases of anorexia nervosa and neurasthenia. The late Dr. William Playfair had the credit of introducing this practice into England. In France the system of *alimentation forcée* is in vogue for similar cases. The main idea is to secure an adequate supply of nutriment in defiance of the repugnance of the patient to consume it. In many cases recourse is had to milk for this purpose. An adult requires about eight pints daily to maintain full nutrition, and this amount is given in divided doses. Beef essence may be combined with this, and less milk given. Confinement to bed is necessary in the Weir Mitchell treatment, and massage is practised twice a day. The patient sees no friends, and holds no communication with them by letters. As a rule, such patients increase in weight and improve in all respects in the course of six weeks, when a return to ordinary diet is gradually permitted, and permission is given to return to society and to resume ordinary avocations. It must be declared, however, that such patients are apt to relapse after a time into their former condition, and may require to undergo treatment a second time. They are commonly unstable creatures, unfit to face the duties and claims of a wholesome life. Some permanent cures are, however, to be expected. Each case is a study in itself.

In some phases of hysteria, and in the treatment of some insane patients, it is necessary to employ forced feeding. This is best carried out by the use of the œsophageal tube by the mouth or by the nasal tube. Rectal injections as a method of forced feeding, strictly so called, are of course unavailable. Koumiss and kephir, being very digestible, are found to be useful in cases of wasting disease, and may be taken and well borne by phthisical patients requiring forced feeding.

In Germany the plan of forced feeding has been much practised in treating phthisical patients in the various sanatoria, but is now, it is believed, less in vogue than formerly. The accounts of it are disgusting to relate, compulsory feeding being enforced till in some cases relief comes only by vomiting. The practice commends itself neither to clinical instinct

nor to common sense. Gross over-feeding cannot possibly be compatible with due digestion or appropriate nutrition. Phthisical patients naturally require the most nourishing food they can fully digest, but it must be a mistake to disgust them by compulsory swallowing of that which they loathe. Moreover, such a plan is not only bad, but it is unnecessary, and is nowhere practised in this country.

Special Dietetic Cures.—There are several of these. The most important is that known as the *Milk Cure.* The diet is limited to milk. As already shown, an adult requires to take from six to eight pints daily to maintain full nutrition. Half a pint is usually taken at a time. It may be given sometimes warm, at others cold; a little sugar may be added to some portions, and a little salt to others. To break the monotony of the treatment, which is apt to prove repellent in some instances, certain flavourings may be added, such as vanilla, lemon essence, or nutmeg. Sometimes it is permissible to add chicken, veal, or mutton broth to some of the milk, which much increases the appreciation and palatableness of the diet. This method of treatment is appropriate for certain forms of dyspepsia, and especially in cases of chronic dysentery and tropical diarrhœa, also in psilosis or sprue. In ill-nourished children with a tendency to pulmonary catarrh, in cases where there is tuberculous predisposition, and in the acute or subacute forms of parenchymatous nephritis, milk cure is sometimes of great benefit. Due care should be taken as to the source of the milk to insure freedom from tuberculous contamination. The treatment is well carried out in some Swiss health resorts. With respect to its application in cases of dysentery, it is important to note that nothing but milk should be administered. The common tendency to add arrowroot or other amylaceous matter to it is to be resisted, and in cases of dyspepsia the ability to digest carbohydrate food must be duly considered. At one time it was thought advisable to treat cases of diabetes by a diet of skimmed milk alone. The patients were found to fare badly, however, and to lose weight and strength, even if they became less glycosuric. The advantage of a milk diet in acute nephritis is certainly great, but it is hardly to be recommended in the more chronic forms for any length of time unless distinct improvement is manifested while under its influence. There is no objection to the admixture in such cases of amylaceous food. The addition of suet is sometimes advisable, especially in cases of chronic tropical diarrhœa, given in the form of the *lac sevi* of the Guy's Hospital Pharmacopœia. Half an ounce of suet melted in an iron spoon is strained through muslin, and added to half a pint of hot milk and intimately stirred. Some powdered mace, cinnamon, or nutmeg may be added for flavouring. Lime-water, to the extent of one-fourth part, may be combined with the milk when the bowels are greatly relaxed. If, on the contrary, there be incomplete digestion of the milk, as shown by the passage of curdy lumps in the stools, the addition of half a drachm of sodium bicarbonate or citrate to the pint is desirable. Barley water may be added, if the milk is too rich in cream, to the extent of one-third of the bulk consumed, and this may

also prevent the clots which are naturally formed in gastric digestion from proving too dense and resistant to the action of the gastric juice.

Predigestion of milk by peptonising may often permit patients to take it when it cannot be borne in a pure or diluted condition. Boiling is found to hinder the ready digestion of milk to a slight extent. Absorption of milk appears to be more complete in young than in older persons.

When milk is disliked or is apt to disagree, much benefit may be obtained from the use of cream, diluted with hot water or barley water. This, however, can never prove a substitute for milk diet, because it cannot be taken in adequate quantity to maintain due nutrition. Malt extract is a valuable addition to milk in all cases of wasting disease, being easy of digestion and nourishing, and milk sugar (lactose) may be also given in some portions of the daily allowance. It may be noted that six pints of milk contain sufficient nutriment for a bedridden adult patient, supplying 2550 calories of energy to the body. For any one leading a more active life, eight pints would be required.

Whey Cure.—As part of the dietary, treatment by whey is practised at several Continental health resorts. Whey can hardly be seriously regarded as a source of nutriment, containing, at it does, little beside lactose, the mineral salts of the milk, and mere traces of proteid and fat. Albeit it has a sufficiently nutritive quality for temporary use in certain morbid conditions. The best method for making whey is to heat thirty ounces of milk to 104° F., and add two teaspoonfuls of prepared rennet to it. The resulting whey (serum lactis) is then to be strained through fine muslin.

During the cure the patient is expected to consume three or four pints of whey in the course of a day, the only other food permitted being fruit or vegetables. Some cases of dyspepsia are treated with smaller quantities, half a pint being taken night and morning. The action is that of a mild laxative and diuretic.

Whey has certainly proved very efficacious in cases of enteric fever where there is reason to suspect deep intestinal ulceration with a tendency to hæmorrhage; and in cases of slight or grave hæmorrhage it is the proper form of nutriment for the patient. In milder cases it is used by some practitioners to the exclusion of milk, as all particles of irritating curd are thus avoided. The patient may be further supported with mutton, chicken, or veal broth, as required (beef-tea or essence being avoided), yolk of eggs, and extract of malt.

In acute nephritis whey is of particular value, its freedom from proteid rendering it harmless to the engorged kidneys and helpful to the general circulation in such cases. Few patients are averse from taking it. To quench thirst in general pyretic conditions, as in pneumonia, when milk and barley water are distasteful, whey may prove very desirable.

Grape Cure.—A method of treatment for various ailments has been in vogue by means of the consumption of large quantities of grapes. Little has been heard of it for the last thirty years. In Switzerland more

particularly has this cure been established. As may be supposed, many pounds' weight of grapes must be consumed to render their effects appreciable. From one to eight pounds are taken in the course of a day between meals, the skins and stones being, of course, rejected. The cure lasts for three weeks. The effect is both laxative and diuretic, and the treatment is alleged to be of use in cases of abdominal plethora and dyspepsia.

It is necessary to have the grapes well washed before taking them. The treatment is best carried out at Vevey, and the season for the cure is during the month of September and the earlier part of October. A light diet is enjoined, with very little animal food.

Salisbury Treatment.—The principle underlying this method consists in feeding patients who suffer from inadequate digestion of amylaceous matters with a diet of proteid matter solely. It was introduced from America, and bears the name of its propounder. As a means of combating acid dyspepsia, arising from imperfect disposal in the stomach and small intestines of carbohydrate food, it has a place as a temporary expedient in certain rebellious cases of this nature. The diet consists of animal food, finely minced, and not too much cooked, in quantities varying from half to three pounds each day. No bread or vegetable food is allowed to be taken. For liquid, hot water is alone permitted. The gristle, fat, and tougher connective tissues must be removed while preparing the meat, and cakes of half to an inch in thickness may be made of this, heated in a pan without water, and cooked till the colour changes. Butter and salt may be added at table. Such a dietary naturally throws a very heavy burden on the kidneys, and for its continuance necessitates a large quantity of water to flush these organs. It can therefore never become a regular method of nutrition, however well it is found to agree with the individual, even if the natural repugnance to this system, especially in women, be overcome. As a temporary expedient, in conjunction with other remedial measures, this method has its place, and may aid in restoration of normal digestive powers, and of nutrition generally, when these have long been in abeyance. Many dyspeptics can digest a meal of proteid with benefit, who are unable to dispose of a mixed meal of proteids and carbohydrates. By an appropriate arrangement of the diet, the end in view may generally be accomplished without recourse to the more crude Salisbury method. In some of these cases it is found that a proteid meal at one time, and a more exclusively carbohydrate one at another, will agree well enough. In health it is found that the work of the digestive organs is rendered lighter when fat and carbohydrates form part of the diet.

The Salisbury treatment has sometimes been found of use in cases of psilosis or sprue, when a purely milk diet, which is best, cannot be borne.

Zomotherapy, or the systematic continued administration of raw meat or raw-meat juice, has recently been employed with success in the treatment of pulmonary tuberculosis by Dr. Philip. It is not a question of

extra feeding, for then cooked meat should have the same effect; this, however, is not the case, as shown both clinically and experimentally by Richet and Héricourt. The important point is that the meat or muscle juice should not be boiled, since the effective constituents, whatever they are, appear to be destroyed in the process.

Diet for the Aged.—In order to arrange a dietary which shall be appropriate for the requirements of persons in advanced life, it is necessary to realise the conditions, in respect of the several bodily functions, which are apt to prevail in aged people. These may be summarised generally as processes of involution, whereby the adequate performance of ordinary function tends to be diminished and the natural powers of the body as a whole are lessened.

In regard to digestion and general trophic processes in the aged, the condition of the heart, arterial system, and the kidneys must be chiefly considered. It is well established that mere age affords no clue to these conditions, men of seventy years of age sometimes manifesting greater integrity of their organs than men of forty. We regard it as a rule that degenerative changes may begin after the age of thirty-five, or after middle life, and these may be commonly expected by the time seventy years are completed. Premature senility indicates a faulty constitution, and is usually inherited. It may also result from faulty habits of life and acquired diseases. Bodily soundness is largely dependent on the healthy condition of the arterial system, and no truer apophthegm was ever uttered than that of the French physician who declared that "on a l'âge de ses artères."

It is recognised that life is commonly protracted in such persons as are spare and lean, and who are small eaters, while gross feeders and obese persons seldom exceed, or indeed reach, the allotted span of three score and ten years. These data afford the key to the subject before us. The main indication is to provide sufficient, and no more, nutriment for persons in advanced life. The vigour of the digestive powers tends to be impaired, and assimilative capacity gradually diminishes as life is prolonged. The functions of the kidneys are apt to fail, mainly as a result of shrinkage in volume resulting from interstitial fibrosis. The former condition necessitates the employment of plain and readily digestible food, duly prepared with reference to the masticatory power of the individual; tender, well-dressed roast meat, mutton, fish or game, finely divided or minced, and well-cooked vegetable food, potato, mashed or passed through a sieve, and spinach being more especially suitable. Panada, lightly boiled eggs, omelettes, and farinaceous puddings are appropriate. Well-prepared mutton broth is useful. When the teeth are defective, and artificial teeth cannot be borne or procured, tripe, ox-palates stewed, fish pudding, and sweetbreads may prove advantageous. Bread and milk, arrowroot made with milk, and gruel, not too thin, are often grateful to the aged.

The condition of the kidneys being ascertained by careful examination of the amount, specific gravity, and qualities of the urine, affords a guide

as to the amount of proteid likely to be borne with impunity ; and the measure of renal inadequacy being gauged, the limit of animal food for the individual is determined. The main portion of the dietary should consist of carbohydrate and vegetable food, to which fish should be added. Such a diet can be presented in a variety of ways, and suffices to meet all the demands of nutrition that can be safely ministered to when the renal functions are inadequate.

It is not uncommon to meet with aged persons who are able to digest and profit by a diet which would be appropriate for men and women twenty years younger. In such cases the bodily powers have been well preserved and the constitution is sound and robust, yet even in these it is incumbent to practise moderation as to quantity, and unsafe to be led into occasional excesses.

In respect of stimulants for the aged, it is safe to affirm that in most cases a regular and moderate amount of good wine is beneficial, at least with one meal in the day. Wine and warmth are proverbially good for the old. From two to six ounces of mature port wine or two ounces of brandy or whisky in the day should suffice. Beyond these limits no more should be taken without prudent medical advice. Tea, coffee, and cocoa are grateful and salutary for the aged. There should be no variety of dishes at any one meal, as a rule, and twice-cooked food is undesirable. The number of meals in the day must vary according to the amount consumed at each, and the ability of the individual to take exercise or be in the open air. If the breakfast is a slender meal, the luncheon may become the important meal of the day, when digestion is probably most vigorous. The evening meal may then consist of farinaceous food, sago, boiled rice and milk, or oatmeal porridge with milk. In many cases there is a gouty habit of body, and this condition has to be met, with special reference to the personal factors of the individual and his experience of the dietary that best tends to avert gouty attacks. No more need be added here than to urge a caution in employing any severe or lowering measures, the object being to raise the general level of nutrition to the highest point attainable by simple and supporting diet, not omitting the use of any wine that can be well digested, or of some spirit in moderate amounts. (*Vide* article, "Old Age.")

It will be understood that nothing recommended in the foregoing article can ever replace the necessarily associated medicinal and other means which are requisite in order to favour restoration to health. Diet may, and can, do much in this direction ; but the clinical practitioner must conduct the dietetic as well as the other therapeutical measures in each case, and if he fail at the same time to *manage* his patient, neither the one nor the other will avail him to promote the highest object of his art, which is to ensure the recovery of the sick.

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THE DIET AND THERAPEUTICS OF CHILDREN

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Although on account of his special constitutional peculiarities the young child bears but a faint resemblance to the fully developed adult, in one respect the likeness is close enough. It is that young children, like their elders, differ curiously amongst themselves not only in general digestive capacity, but also in their individual ability to assimilate this or that kind of food. One baby thrives upon fare which is innutritious if not actively hurtful to another; so that to prescribe a dietary for a young infant is to engage in an experiment which, if it do not succeed at once, may require many changes in detail before it can be brought to a successful issue.

So long as the infant can be fed from the breast all is likely to go well; for in human milk he meets with a digestible and amply nutritious fluid which he swallows straight from the gland, pure and uncontaminated by germs. There are few children who do not thrive when thus fed, provided, of course, that the supply of milk be sufficient and its quality good. But so many mothers are unable to nurse their babies that a large proportion of infants have to be brought up by other means. The problem is to imitate the natural food of which the child has been deprived. The more closely this can be done the better the prospect of rearing the infant with success.

To be accurately adapted to the wants of the infant, the required

food must contain all the elements of nutrition as nearly as possible in the proportions observed in human milk; it must be well within the powers of the stomach, so as to leave little undigested residue to ferment in the bowels and be a source of mischief; it must be fresh and in good condition; and, lastly, to be a perfect food, it should contain a sufficient proportion of the vitalising element — whatever that may be — which endows it with its antiscorbutic properties. Now, milk contains in itself all the elements of nutrition; and the milk of many animals approaches human milk in composition more or less closely. Any of these may be used; but practically we are forced for convenience' sake to fall back upon cow's milk, which is always at hand; and this can be adapted to our purpose without much difficulty.

As compared with human milk,[1] the milk of the cow contains a larger proportion of curd, but is deficient in sugar and to a small extent in fat. To bring it, then, to the standard of human milk it must be diluted and sweetened. But this is not enough. The curd of cow's milk coagulates in one large, tough lump which resists digestion; while that from the human breast forms a light, loose clot which is easily penetrated by the digestive fluids. When, therefore, cow's milk is used, steps must be taken to prevent this firm clotting of the curd. If we add to the milk some thickening material the particles of curd are kept apart, so that when the casein coagulates in the infant's stomach by the action of the gastric juice the clot consists, primarily at any rate, of a multitude of little lumps of curd instead of one solid mass. For the thickening material some form of starch is often used; but as this is difficult of digestion by the young child, barley water is to be preferred. Barley water itself contains starch, but in comparatively small quantity and very finely divided. It rarely disagrees, and when mixed with a fourth part of milk suits the large majority of new-born infants. The meal should be sweetened with white sugar; and it is important that the barley water should be freshly made, for it cannot be given with safety if more than six hours old. If the cow's milk be used uncooked as it is delivered to the house, it retains all its antiscorbutic properties: on the other hand, in this state it is probably loaded with germs of various kinds, which may indeed be harmless, but may be capable of exciting dangerous fermentations, or conveying the seeds of serious disease. Epidemics of diphtheria and scarlatina, as well as bowel complaints of great gravity, may owe their origin to impure milk. Unfortunately boiling the milk renders it less active as an antiscorbutic: but it is wiser to make this sacrifice for the sake of avoiding the greater evil, and to use milk which has been boiled or sterilised. If the latter, it is best to add the barley water to the milk before sterilisation,[2] and to

[1] For purposes of comparison, Dr. V. A. Meigs' (1) analysis is subjoined:—

	Water.	Sugar.	Casein.	Fat.	Ash.
Woman's milk	87·163	7·407	1·046	4·283	·101
Cow's milk	88·549	4·898	2·792	3·310	·451

[2] Milk sterilised in the house by Sohxlet's apparatus is greatly to be preferred to that supplied by a company.

allow the child to suck the mixture from the sterilising bottle fitted with a mouthpiece.

This method of feeding is to be preferred to the common plan of giving milk and water alkalised with a third part of lime-water. The lime-water acts by partially neutralising the gastric juice, so that a considerable proportion of the milk passes uncoagulated from the stomach and is digested in the bowels. Healthy babies doubtless often thrive upon this food, although thus deprived of a very important agent of digestion.

It may happen that the new-born infant has a special inability to digest fresh cow's milk. In that case he will often do well for the first few months upon condensed milk and water; but cow's milk sterilised and thickened with barley water should be tried again after an interval, varying the proportion of milk in the mixture to suit the child's digestive capabilities, for an infant who is greatly overtaxed by a third part of milk may digest a sixth with ease. No effort should be spared to enable the child to digest the fresh milk, for condensed milk is a very undesirable food for him after he is three months old. In all cases of difficulty, cow's milk peptonised in the house should be tried, and will often agree. We should also never fail to inquire as to the cleanliness of the feeding-bottle and the times of feeding. Much may often be done by careful regulation of these matters.

The temperature of the meal should be 95°, and the food can be easily warmed to this heat by placing the bottle in a small basin filled with hot water. The quantity given in the first week should be a couple of ounces, but more will very soon be required. The regulation of quantity is a matter of small importance. If a proper interval be allowed for digestion, the quantity taken at each meal may be left safely to the child himself. A very young baby can be trusted to stop sucking when he has had enough, and any excess which may have been swallowed is usually regurgitated without effort shortly after the meal.

Children may do well for the first six months upon milk and barley water alone without any change; but often they require more variety in their food: in all cases where the digestion is difficult, and has to be humoured, variety in the diet is too important a stimulus to be neglected. Sooner or later, then, the question of "Infants' Foods" has to be considered. All these are preserved or tinned foods, and therefore destitute of antiscorbutic properties. On this account they are only allowable as aids in the diet, for cow's milk, when this can be borne, must always be our mainstay.

The tinned foods may be divided into four classes, viz.—

1. Milk evaporated to dryness or concentrated to the consistence of thick cream and preserved with sugar or malt.

2. Milk desiccated and mixed with partially converted starch.

3. Foods consisting of wheaten flour more or less completely digested or mixed with malt or pancreatine.

4. Foods consisting merely of the flour of some cereal baked.

All these, as foods, leave something to be desired; for while none of them possesses antiscorbutic properties, all are found in other respects to be faulty as nutritives. According to the analyses of Dr. A. Stutzer (2), of Bonn, most are lacking in fat; and in many the amount of proteid is too small and its proportion to the other nutritious matters too narrow. Some are weak in bone-forming material; others contain insoluble carbohydrates (unconverted starch) in excessive quantity, and therefore trying to the digestive capacities of an infant. But although beneath the standard of perfect nutrients, and ill fitted to be for long together the sole nourishment of a young child, these foods are by no means useless. As additions to the cow's milk, providing supplementary nourishment, furnishing material for flattering the palate and giving variety and relish to the meals, their value is great. For infants who cannot digest fresh cow's milk we find in the foods containing desiccated and condensed milk a fair temporary substitute; and even if the inability prove permanent, we can often by this means and a little management maintain the child in a fair state of nutrition until he is of an age to supply the deficiencies of his dietary by other means.

The choice of the food is of great importance. Class I., which consists of milk alone as a syrup or dry powder, should be reserved for the first three months of life. Dr. Rotch (3) advises that these milks be diluted with nine parts of water, and that 20 per cent of cream be added to supply the deficiency in the fat, but this proportion is a high one and makes the food too rich for many children. These do better on no more than half the quantity of cream recommended. The only other tinned food allowable at this age is Mellin's Food, which belongs to Class III. In this the starch is almost completely predigested and converted into dextrin and maltose. One or two teaspoonfuls may be added to each alternate meal of milk and barley water for the sake of giving variety. Starches are to be used for infants below the age of six months with great caution. The secretion of saliva is very small for some time after birth, and does not become free until the third month; and the pancreatic secretion is very scanty for the first six months of life, and does not acquire its full amylolytic action for some months longer. Up to the age of six months starch should only be given when guarded with a digestive, as in the malted foods or Benger's pancreatic food. Later it may be tried cautiously and in small quantity without this safeguard, in the form of baked flour or a rusk, but always with milk. Any of the foods in Class IV. may be used at this time.

The child should be fed every two hours for the first six weeks; then the interval between the meals can be gradually increased, and the meals themselves made larger and more satisfying. When a tinned preparation is used it must not be added to the milk until the meal-time comes round, for a food allowed to stand ready made quickly begins to ferment.

It would be out of place here to refer to the various derangements which may affect the hand-fed infant, or the changes in the diet which

such disorders require. The reader should consult special treatises for information upon these important points. It will be sufficient to state, as a general rule, that whenever digestion is difficult and the nutrition of the child unsatisfactory we should aim at plenty of variety in his meals; that we should not persevere with a food which is found not to agree; and that as cooked milk is weak in antiscorbutic properties, we must be always on the watch, while using it, for early signs of infantile scurvy. It may also be remarked that healthy digestion depends in a great measure upon the general management of the infant. Soiled linen should be removed from the nursery without delay, and the room should be frequently ventilated so as to keep the air fairly pure. Great attention, too, should be paid to warmth of the child's feet and legs, especially when he is taken out of the house for his daily airing; and the washing of his body should be carried out as quickly as possible and without undue exposure. An infant whose feet are habitually cold never has a good digestion; and many a fatal attack of gastritis has owed its origin to a chill contracted by careless exposure in or after the daily bath.

At the end of the first twelve months the infant may be allowed for his dinner some weak veal or chicken broth thickened with barley and strained. On alternate days he may take the yolk of a new-laid egg lightly boiled or beaten up with milk. At this time it is advisable to accustom the child to take food from a cup or spoon, so as gradually to wean him from the bottle; and when he enters upon his second year a light pudding made from sponge cake or rusk may be given two or three times a week.

Meat must not be allowed until the child is sixteen months old: he may then begin to take a little underdone mutton chop. At first this should be pounded in a mortar and rubbed through a wire sieve; but after a month or so it will be sufficient to mince it very finely. It is important that all changes made in the diet be made cautiously and with judgment. A time should be chosen when the child is happy and cheerful, digesting without trouble and sleeping quietly, and the new food must be given in small quantity at first. A change made when the child is teething or fretful or restless at night is hardly likely to be attended with success. At first, meat should be given twice a week only. On other days the dinner should consist of strong soup with some well-boiled vegetable, such as cauliflower, vegetable marrow, or tender French beans. Once or twice a week the child may take some chicken or boiled fish. Potatoes are not to be allowed every day; and batter pudding and puddings made from bread and rusk are to be preferred, as less purely farinaceous, to rice, sago, and tapioca; although the latter are, no doubt, sanctioned by nursery tradition and prejudice. But an excess of starch in their diet is to be avoided for growing boys and girls. At no time of life do young children find the digestion of starch an easy matter; and it is unwise to overload them with a food which fattens but gives little strength, and is but too apt to make them lethargic and dull.

Beef and mutton, as a rule, they can digest without difficulty. I have been told many times that this or that child could digest no meat, but have almost always found that it was not the meat, but the potato eaten with it which disagreed. Cold meat, again, is as harmless as hot; and minces and hashes are not to be withheld from children through any groundless fear of "twice-cooked" meat. Nursery superstitions, like other delusions, die hard; but dishes in which the meat is merely warmed through without being really cooked a second time are innocent enough. At all ages variety in diet is to be aimed at; and ham and tongue (thinly sliced) and bacon for breakfast help to lighten the monotony of the daily meals and stimulate the digestion as well as gratify the palate.

A word may be said as to the arrangement of the meals. Arbitrary custom ordains that the two substantial meals of the day—the breakfast and dinner—must be confined to six hours out of the twenty-four; and that for the remaining eighteen hours the child must take nothing but milk and bread and butter, with the addition, perhaps, of cake or a little jam. This arrangement answers fairly well with sturdy subjects who can be prepared with an appetite at the prescribed times, although even with these a more rational distribution of their food is to be preferred. But many children, especially those who are anæmic and fragile, cannot thus be hungry at command. Often in the forenoon they do not care to eat at all. They hardly touch breakfast, and only trifle with the mid-day dinner. Towards evening, however, the appetite improves, and at five or six o'clock they would eat a hearty meal if allowed to do so. For years in these cases I have adopted the plan of ordering a substantial meal towards the end of the day, at the time when the child is best disposed to take it; and if the more fermentable articles, such as sweets and potatoes, be excluded from the menu, and a good hour before bedtime be allowed for digestion, I have rarely found the patient anything but the better for the change. In these cases a little stimulant is often a help in improving the appetite and aiding digestion. It should be given with the principal meal. I often order the St. Raphael wine, but any sound wine will usually agree, provided it be not acid. I think a good Burgundy is to be preferred to a claret. Alcohol must be regarded strictly as a medicine in the case of a child, and is not to be ordered except to serve a temporary purpose. It has no tonic properties, and must be discontinued when the appetite improves.

Diet enters so largely into the treatment of children's diseases, and the rate of recovery may be so influenced by a judicious selection of the food, that an intimate acquaintance with these matters is indispensable to success as a practical therapeutist. Children, especially young children, are more dependent than adults upon a daily supply of nourishment, and suffer more in proportion if this be withheld. The digestion fluctuates from day to day in strict relation to the general health; and flags at once when this is impaired. In acute disease with a high temperature the digestive power is very limited, and in order that the nutritive supply be not cut off altogether, the food provided must be of the lightest and most

digestible kind. But "light" food is not to be taken to mean farinaceous food. Starches, especially when cooked with milk, are ill-suited to such a condition, and must be given, if given at all, with great caution, or they may do harm. As a thickening material for broth they are more useful, and beef-tea thickened with tapioca or arrowroot will often agree when a common tapioca pudding only excites discomfort from acidity and flatulence. It is important to realise early that rice and sago and such-like puddings are not "light" or easily digestible foods; and that to task a disordered or weakened stomach with such highly fermentable material in a case of acute illness, or during an early stage of convalescence from grave disease, is to aggravate the symptoms and seriously retard recovery. In the dieting of febrile diseases in the child the rules which regulate the hand-feeding of infants should be observed. Starch should not be given with milk unless guarded by a digestive; and milk itself, if not peptonised, must be thickened with barley water or gelatin. The meat jellies and cold extracts of meat agree well with children beyond the age of infancy, if not given too liberally. The quantity allowed in each case is to be determined by the strength of the child and the state of his stomach. A rise of temperature, disturbed sleep, or discomfort after the meal, may be taken to show that the quantity must be reduced. So, also, if during convalescence the urine be habitually thick with lithates, it is usually a sign that the patient is being over-fed.

It is often curious to note the immediate improvement which takes place in the condition of a sick child when an excessive dietary is reduced, and the food both in quantity and quality is adapted with judgment to the enfeebled powers of the patient. But it is not enough to see that nourishment is assimilated with little effort; we have also to take care that waste products are freely eliminated; that the bodily heat, if excessive, is controlled; and that the skin, the kidneys, and the bowels are encouraged to the full discharge of their duties. Moreover, we must be careful to enforce proper rest, and to have the air of the room maintained at a suitable temperature and frequently renewed.

Baths.—The constitutional peculiarities of the young child have an important bearing upon the treatment of disease in early life. The curious sensitiveness of the nervous system gives an especial value to counter-irritants of the skin and external applications generally. Amongst these remedies baths take the first place. The hot bath (100° F.) is an important general stimulant in cases of extreme depression either from hæmorrhage, profuse diarrhœa, vomiting, pulmonary collapse, severe nervous shock, or any other depressing agency. When used with this object, the child must not remain longer than three or four minutes in the hot water. This bath can be made more stimulating by the addition of flour of mustard in the proportion of one ounce to each gallon of water. The mustard is first mixed into a paste with cold water, and is then squeezed through a piece of fine muslin into the bath.

The warm bath (90° F.) calms excitement, allays spasm, and induces sleep. It is useful in cases of reflex convulsions and every form of

nervous agitation. Its diaphoretic action makes it of great service in Bright's disease, especially if the child be afterwards wrapped in blankets to keep up the action of the skin. The duration of the warm bath should be from fifteen to twenty minutes.

The cold douche (65°-70° F.) is only useful in the morning before breakfast. If given rapidly it is a bracing tonic for children in whom the system responds readily to the shock. Even pallid, delicate subjects derive great benefit from it if proper precautions be taken to promote a healthy reaction. In the case of a weakly child the patient should be first rapidly sponged in a hot bath (100°), and should receive the douche as he sits in the hot water. Immediately afterwards he should be wrapped up undried in a hot blanket, and returned for a few minutes to his bed. Reaction is hastened if the child drink a cup of hot milk ten minutes before being put into the water. This is the only way in which cold or nearly cold water can be used to advantage with children whose nutrition is at fault. The cold sponging so often employed is highly objectionable for such patients on account of the long exposure it involves. Even when the douche is used as described above, its temperature must be carefully adjusted to the readiness of reaction shown by the patient. Some children respond best to a comparatively low temperature, while others, whose power of reaction is slight, require a douche of 75° or even 80°, and are depressed instead of strengthened if the water be colder.

There is another method of using water externally which is sometimes of the highest value. In cases of ptomaine poisoning, with or without vomiting or diarrhœa, the skin loses its elasticity more or less completely, so that when pinched up it lies in loose folds upon the abdomen. This state of skin is probably a sign of imperfect action of the kidneys, for the urinary secretion at the time is almost invariably scanty, and is sometimes suppressed. At any rate, unless the elasticity of the skin can be restored, the patient will almost certainly die. It is my custom in these cases to pack the child in a large towel wrung out of cold water, or of water containing a sixth part of eau de Cologne or brandy, and to keep him well covered and packed in with many blankets for hours together. At the end of every three hours the child is unswathed, rubbed dry, and repacked as before. After some hours of this treatment the kidneys begin to act more freely and the skin to recover its elasticity. I have kept young children thus packed for twenty-four hours together, with the very best results; for if by this means the elasticity of the skin return, the prospects of the child's recovery are very materially improved. This form of blanket bath should be reserved for cases where it is desired to increase the action of the skin or kidneys. It cannot be relied upon to lower the temperature when this is high; for unless the process set up copious perspiration, the heat of the blankets increases the pyrexia instead of lessening it. Children as a rule bear high temperatures well; but if the bodily heat exceed 105° steps must be taken to reduce it. The plan I prefer consists in wrapping the patient in a sheet wrung out of cold water, and covering merely with another dry sheet. Under this treat-

ment the temperature quickly falls; and if the pyrexia has been accompanied by convulsions or great excitement, the nervous disturbance, as a rule, quickly subsides, and the child sinks into a quiet sleep.

Counter-Irritation.—Of the baths above described the hot and mustard baths may be considered as counter-irritants and general stimulants. Children respond well to counter-irritation, whether this be used generally or locally. In cases of bronchitis or catarrhal pneumonia, long-continued counter-irritation with mustard poultices diluted with four or five times the quantity of linseed meal, and thoroughly mixed, is of the utmost service. A large weak poultice kept on the skin for six or eight hours is to be preferred, as a rule, to a stronger application used for a shorter period; but in cases of imminent danger, where an immediate effect is required, a mustard leaf or even dry-cupping of the back will often produce speedy relief. Mustard leaves, however, and violent applications such as blisters, are not to be recommended in the case of babies and the younger children, and must be used with caution even with older subjects who are cachectic or ill-nourished; for troublesome ulcerations or even gangrene of the skin are occasionally seen to follow their use. Moreover, it must be remembered that a blister is equal to a burn of the third degree, and may have a seriously exhausting effect upon a weakly child. In a properly selected case, however, the value of this form of counter-irritation is great. In peri- and endo-carditis no time should be lost in having recourse to it. I believe I have often succeeded in cutting short an attack of pericarditis by a timely blister; and the value of a vesicant in promoting absorption when the pericardial sac is full of fluid admits of no reasonable doubt. In such a case, when used to a young child, the blister must be of small size, and must be kept in contact with the skin for a short time only. Thus it can be applied for two hours to a child of three years old, and half an hour longer for each additional year of life. If the blister have not formed when the irritant is removed, a bread and water poultice will soon cause it to rise up. In cases of exceptional delicacy of skin a sheet of oiled tissue-paper may be interposed between the blister and the surface to be acted on, as recommended by Bretonneau.

Frictions of the skin with almond oil or stimulating liniments are useful in various conditions. Threatened collapse of the lung may often be averted by this means; and if it has already occurred, persevering friction with strong counter-irritants may do much in helping the lung to re-expand. In whooping-cough the use of rubefacient embrocations is held in high esteem as a domestic remedy; and in all cases of chronic disease friction of the surface combined with systematic massage of the muscles has a general as well as a local value. In chronic digestive derangements the skin is often dry, scaly, and inactive. For this condition the application of warm almond oil becomes a useful resource. The patient is first well sponged in a bath of hot soap-suds, then quickly dried, and freely anointed all over the body with the warm oil. He is then put to bed in a flannel night-dress or wrapped in a blanket. The

efficacy of a few repetitions of this treatment in improving nutrition and making the skin soft and supple is remarkable.

Stimulants.—Children are very easily depressed by acute disease, so that it is important to watch for early signs of failure. On this account alcoholic stimulants take a high place among internal remedies, and a few doses of this medicine will often in a few hours completely alter the aspect of a case, and turn the scale in favour of recovery. In chronic disease, also, the effect is equally beneficial. It is a matter of common observation at the East London Hospital for Children that the young patients who are enfeebled and wasted by privations of all kinds, combined with long-continued ill-health, often make no response to the action of drugs until their exhausted energies have been revived by a few doses of wine or brandy.

Tonics.—The rapidity with which nutrition suffers in early life, when any hindrance arises to the easy assimilation of food, gives great value to all invigorating remedies. But tonics are not to be ordered indiscriminately. It is of little use to prescribe iron or the mineral acids for a sickly-looking child merely because he is anæmic and weakly, and leave unnoticed a chronic gastric derangement which is the cause of his poor appetite and feeble digestion. The dyspepsia must first be treated with alkalis and stomachics, and by a judicious limitation of the more fermentable articles of food, before tonics can be given with any good result. As the digestion is liable to suffer in all the ailments of childhood the alkalis are perhaps the most useful of our remedies. By this means we check the excessive secretion of mucus and neutralise acidity. Moreover, the addition of an antiseptic, such as spirits of chloroform, and of warming aromatics, arrests fermentation and reduces flatulence. At this period of life, whenever alkaline remedies are prescribed, an aromatic, such as cinnamon, dill, or peppermint, should always be included in the mixture.

When tonics are given the dilute nitro-hydrochloric acid is very useful with small doses of nux vomica; and children take quinine with great benefit if the dose be not too small. After any of the infectious fevers quinine is always indicated. A child of twelve months old will take a grain three times a day; and a grain may be added for each year of the child's life until a dose of 5 grains is reached. This can be given three, four, or six times in the day as may seem desirable. The usual doses ordered for children are too small; for young patients are not at all susceptible to the alkaloid, and rarely suffer from cinchonism. Cod-liver oil is the favourite remedy for every form of wasting or pallor, but the oil is only useful when the digestion is in fair order, and should never be given to a bilious or dyspeptic child. It is usually administered in quantities far too large. A child of twelve months old can rarely digest more than 10 drops at one time, and a teaspoonful should be the maximum dose at any age.

The dosage of medicine for children is often a cause of some perplexity. Of certain drugs they show a curious tolerance. Belladonna

they can take in large doses, for although a few drops of the tincture may bring out the characteristic rash, this is not a symptom of excess, and has no relation to the size of the dose. To opium, as is well known, they are keenly susceptible. It is wise to prescribe this narcotic in very small quantities, but to repeat the dose as frequently as may be necessary. If this be done, and we give directions that the child is never to be roused up to take his medicine, we need have no fear of his becoming narcotised. In connexion with this subject it may be remarked that infants who are being drugged by unscrupulous nurses with "soothing syrups," or other opiates, invariably show it by symptoms which are characteristic enough to the experienced eye. The child lies in a drowsy state with contracted pupils, he often vomits, his bowels are obstinately confined, his water is scanty, and his skin is curiously inelastic. If this combination of symptoms be noticed in a young baby, we have the strongest reasons for suspecting the secret administration of a narcotic. For children who suffer from abdominal pains codeina is a better sedative than opium, especially as it has the advantage of not interfering with the regular action of the bowels. A baby of one year old will bear well one-twenty-fourth of a grain of the alkaloid three times a day.

Antipyrin, like quinine, children take well; and arsenic may be given to patients of four years old and upwards in the dose usually prescribed for the adult. The iodides, again, are well borne in early life, and may be given in large doses without fear of producing iodism. In the usual 1- and 2-grain doses the drug seems to produce very little effect; it must be pushed boldly to be of service. I look upon 10 grains three times a day as by no means an excessive dose for a child of four or five years of age. Ergot I have given for weeks together in large quantity in the treatment of chorea. The liquid extract in doses of 60, 90, and 120 drops, given every two, three, or four hours in the day and twice in the night, I have found quickly to moderate the unruly movements without producing any feeling of discomfort in the patient. A reduction of the pulse-rate by about twenty beats is the only physiological effect that I have noticed. In smaller doses I have continued the use of the drug for months together. In epilepsy 30 drops of the liquid extract with or without a drop or two of liq. strychninæ may be persisted with for many months at a stretch without any fear of ill consequences; and given thus I hold the remedy to be one of the utmost value. Recently I have been using ergotine instead of the liquid extract, as a less bulky preparation, and one less likely to vary in strength. I give it in doses of 5 to 12 grains every two, three, or four hours to children of any age in cases of chorea. Chloral is another remedy which is well borne in infancy and childhood, and this fact should be remembered in prescribing for the spasmodic disturbances, such as laryngismus. A grain every three or four hours may be safely given to a child of six months old. Still, in using this narcotic, as in the case of opium, it is advisable to caution the nurse against giving the medicine to a drowsy child. With all such remedies minute frequent doses are to be preferred to a

larger dose given less frequently. In this connexion it may be mentioned that there is one drug, although of a different class, which should be avoided. Acetate of lead given internally is, I believe, sometimes a cause of convulsions in infants and young children, and I look upon it as a highly dangerous remedy for a young patient.

The making of drugs palatable to young children is far from easy. The bitterness of quinine it is impossible to disguise completely; but it may be modified by giving it suspended in glycerin and water. Nauseous powders are best given in "cachets"; and young children soon learn to swallow them. It is wise to avoid the use of syrups for sweetening purposes: there are few illnesses in young people which are not complicated by a certain amount of gastric disturbance; and the quantity of sugar contained in the syrups must provide additional material for fermentation, and excite acidity and flatulence. There is no doubt that the medicated syrups, which are manufactured so largely, are often the cause of great discomfort to the patient, if not of worse evils; the stale syrup, by increasing the digestive derangement, may be more productive of ill than the drug dissolved in it is of good.

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E. S.

PRINCIPLES OF DRUG THERAPEUTICS

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I. INTRODUCTORY

THE work of the great Italian anatomists, Vesalius, Fallopius, Eustachius and others, in the latter half of the sixteenth century, led eventually to the overthrow of the Galenic system of drug therapeutics; but the influence of the anatomists in this direction was by no means immediate. The early editions of the London Pharmacopœia, which was first published in 1618, probably indicate fairly well the method on which drugs were used in England at that day for the cure of disease. In that of 1632 most of the formulæ are copied from the works of Greek and Arabian physicians,—from Galen, Avicenna, Razes, Haly-abbas, and Mesua,—the name of the physician being given in each case at the head of the formula. Some, however, are of more modern date; John of Arderne

(1370) is responsible for two compounds, and from Fernlius many are derived. We note many substances and processes introduced by the alchemists; vitrum antimonii and acetate of lead, for example, are amongst the remedies, and several of the preparations are made by distillation. We also see the influence of the discovery of the New World on medicine, for guaiacum, cubebs, sarsaparilla, and sassafras are amongst the official substances. There is a great variety of compounds; almost all are very complex, many of them containing 30 to 50 ingredients; into the "Antidotus Magna Matthioli Adversus Venena et Pestem" there enter 131 ingredients. There was certainly no lack of curative agents; in the list of simples we find 160 roots, 30 barks, 16 woods, 220 herbs, 90 flowers, 96 fruits, 136 seeds, and 50 gums; besides juices and some other special parts of plants. The animal kingdom furnished 190 items. The fat of 22 animals, the excrement of 11, and the urine of 5 occupy places in the official list of remedies; man is included in each case. Sweat was an official remedy, so too were the ossa triquetra of the human cranium. The brains of the leopard and of the sparrow, the lungs of the fox, and the body of the viper are found among the official animal substances. Sixty syrups and 180 waters were official.

The discovery of the circulation by Harvey, and the advances made in the knowledge of the structure and functions of the body by Willis, Glisson, Malpighi, and others, together with the advancement of chemistry and physics, led, during the seventeenth century, to the formation of new hypotheses concerning disease and its treatment. Van Helmont taught that life was connected with the presence in man of a kind of personal spirit (Archeus), which from its seat in the epigastrium presided over the functions of the body. This Archeus sometimes went wrong, owing to external or internal influences, hence diseases arose. Later we find chemical and mechanical conceptions of disease. By Sylvius and Willis acidity and alkalinity, or fermentation in the fluids of the body, were supposed to cause disease; whilst Baglivi and other Italian observers, and still later Archibald Pitcairn in this country, laid chief stress on the mechanical changes connected with the tissues and the circulation as causes of disease. All the advocates of these hypotheses either contributed something to the knowledge of the treatment of disease by drugs, or by their works instigated further inquiry: to Willis and Sydenham we owe the greatest advances.

Willis was one of the first to lay stress on the importance of a knowledge of the structure of the different organs as a guide to the use of drugs; and in his *Pharmaceutice rationalis* (1676) he first gives an account of the minute structure of the alimentary canal and its various parts, and of the arteries; he then describes the action of emetics, cathartics, diuretics, diaphoretics, cordials, hypnotics, and opiates. Further on he deals with the lungs and bronchial tubes, and the changes in respiration in diseases such as phthisis, hæmoptysis, and other lung ailments, giving the indications for treatment and the remedies which in his opinion answered these indications. He likewise points out what he regards as the rational

treatment for jaundice, ascites, tympanites, and anasarca. In a third portion of the work he deals with the causes and treatment of hæmorrhage, and with blisters, issues, etc. The practical outcome of the work of Willis was of less value than the spirit of his teaching; his pathological ideas about animal spirits and fermentation as causes of disease were very crude; he was much influenced in his conclusions by old hypotheses of the action of morbid materials, and the indications of the qualities (heat, cold, etc.) of drugs; above all, he too readily supposed that the drugs under which his patients recovered had cured them. His prescriptions are complex, and contain not only a large number of useless agents, but such remedies as the human skull, viper's flesh, millipedes, etc. Yet when he dealt with subjects controlled by anatomical knowledge, he made valuable additions to the existing therapeutical means.

Sydenham professed to recognise the value of anatomical knowledge, but we find little of it in his work. Like Hippocrates, he sought to aid the natural progress of those changes or "commotions" in the blood and fluids of the body which he regarded as the causes of acute disease, and to help nature in her struggle to remove morbid matters. He advocated the removal of the immediate causes of disease, but had no belief in the possibility of dealing with remote causes. By close observation he attempted to determine definite lines for the administration of drugs; he also sought to discover specific remedies, such as he held cinchona to be for ague. He preferred vegetable drugs to animal or mineral, because the animal are too like, and the mineral too unlike the tissues of the body. His prescriptions were more simple than those of Willis, and they are almost free from absurd constituents. But if we examine the prescriptions of both Willis and Sydenham we cannot but see that, with the exception of emetics, purgatives, bitters, and carminatives, very few of the drugs they used had the powers which were claimed for them; and that the art of medicine suffered no loss when a large proportion of the drugs in which they had faith was consigned to oblivion. In such circumstances we cannot be surprised that the Pharmacopœia of the middle of the seventeenth century showed no signs of improvement. In that of 1677 we find the drugs and compounds almost as numerous as in the Pharmacopœia of 1618; indeed, some of the remedies in the latter are even more extraordinary than any in the earlier Pharmacopœia. Not only is human urine set forth as a remedy, but care is taken to distinguish Urina hominis pueri impuberis from Urina hominis adulti! But it is to be remembered that urine resembles beef-tea in containing the products of nitrogenous waste. The urine of boys on a more farinaceous diet may differ very considerably in its composition from that of adults on diet containing abundance of flesh. Urine is still used in India for the same purposes as we use beef-tea. It is interesting to note that in this Pharmacopœia we find for the first time jalap, serpentary, digitalis, and cinchona; and that the names of Galen and the Arabian physicians cease to appear at the head of the formulæ copied from their works.

At the end of the seventeenth century the hypotheses of Boerhaave, Hoffmann, and Stahl considerably influenced therapeutic practice. The two former looked on health and disease as the outcome of chemical and physical conditions acting on tissues endowed with vital properties, which Hoffmann thought due to the presence of an ether-like fluid existing both in the solids and the blood; Stahl attributed everything to soul or spirit. Though both Boerhaave and Hoffmann looked upon the solids of the body as playing an important part in disease, they did not consider them as alone concerned. The former, holding that acridity or viscosity of the humours shared in the production of disease, prescribed medicines with the view of rendering them less viscid; the latter, though attributing disease chiefly to excessive or defective contraction of the solid tissues (spasm or atony), nevertheless prescribed alteratives for the humours, and evacuants for defective excretions. Stahl, on the other hand, was led by his animistic views to deny the efficacy of medicine almost entirely: he even threw doubt on the use of opium and cinchona bark. Though all these eminent men, and many others, added something to the general fund of knowledge concerning therapeutics, the treatment of disease by drugs improved but slowly, and was dominated by strange conceits and superstitions.

Scorpions, earthworms, woodlice and viper's flesh, the excrement of the dog, goose, horse, and pigeon appear in the Pharmacopœia of the Royal College of Physicians of London of 1721. The formulæ were somewhat less complex than in the previous century; but one, "Mithradatium," contains 49 ingredients; another, "Theriaca Andromachi," 63, including viper's flesh; and one of the Confectiones, 50, amongst which appear bezoars, corals, pearls, and the flesh, heart, and liver of the viper. In this connexion it is interesting to note that the bile of venomous snakes has been found by Sir T. Fraser to contain anti-venin.

Amongst the drugs which appear for the first time are the following:—Canella alba, tartar emetic, secale cornutum, stramonium, gamboge, ipecacuanha, and senega. Chemical knowledge had not reached the physicians, for the minerals are still divided into sulphurs, salts, and earths; arsenious acid being included among the sulphurs. Twenty-five years later the Pharmacopœia of the College of Physicians indicates a considerable change. The compounds are much simpler, and with a few exceptions they are not unlike those of the present day in the number of their ingredients. The Mithradatium, however, still contains 46 ingredients, and the Theriaca Andromachi 62. The long list of animal substances has disappeared, but a few extraordinary materials are still met with: crab's claws, the so-called "crab's eyes" (which consist of a mixture of calcium carbonate and calcium phosphate now contained in a pure form in the present Pharmacopœia), viper's flesh (in an ointment), bezoars, woodlice, and red coral are still official. On the other hand, some useful remedies seem to have dropped out. Nux vomica, digitalis, senega, hyoscyamus, stramonium, male fern, and secale cornutum are no longer official. Spirit of nitrous ether is official for the first time. A large

number of useful oils are introduced, and the chemistry is much more advanced.

During the latter half of the eighteenth century very great advances were made in all the sciences bearing on medicine. Haller founded Physiology. Chemistry had advanced greatly. Barthez, in France, put forward a more tenable vitalistic conception of the nature of disease, and Cullen's Materia Medica was in every respect a great advance on any which had preceded it. The London Pharmacopœia, published in 1788, and that of Edinburgh, which appeared in 1780, reflected the rapid advance of knowledge in Physiology, Pathology, Chemistry, and Medicine which now occurred. The excessively complicated formulæ, which the older Pharmacopœias contained, were swept away. The numerous absurd animal substances present in previous Pharmacopœias were almost entirely omitted. Digitalis, senega, and male fern recovered their place in the London Pharmacopœia; and cascarilla, kino, calumba, and quassia were introduced.

The last years of the eighteenth and the first years of the nineteenth century were marked by a fresh outbreak of hypotheses concerning the cause and cure of disease, which had, for the time being, a considerable influence on the treatment of disease by drugs.

Brown, a pupil of Cullen, maintained that the tissues of the body possess excitability; that life is the outcome of the action of stimuli, such as warmth, food, etc., on this excitability, which is uniformly diffused in all tissues; that sthenic diseases are due to excessive, and asthenic to defective excitement. All remedies are stimuli, and only differ in their power. Strong stimuli, such as opium, musk, ammonia, and camphor, are useful in asthenic diseases; but, if given in excess, they may, by producing over-excitement, lead to debility: other substances, such as purgatives, emetics, etc., produce less excitement than is requisite for health, and are antisthenic or debilitating. Brown held that, for the most part, diseases are asthenic, and his treatment therefore consisted chiefly of stimulants. He looked upon sthenic and asthenic conditions as affecting the entire economy, and took little note of local changes, holding that excitability is uniformly diffused; and that it cannot be augmented in one part only, for then it would be unevenly distributed. This doctrine was largely accepted, and modifications of it were promulgated both in Italy and in France.

Rasori held views not unlike those of Brown. Broussais also taught that life is due to stimulation; that to live is nothing else than to be excited: but he considered that different diseases possess different degrees of excitability; and further, that as the sum total of excitability in the body is always the same, augmentation in the one part occasions diminution elsewhere. He looked upon all medicines as either stimulants or debilitants, but strongly upheld the view that all so-called general diseases have a local origin. Fevers, for instance, he believed to depend on gastro-intestinal inflammation. He classified medicines as debilitants, direct stimulants, and revulsives; and, like

Rasori, he looked upon undue irritation as the cause of most diseases; practically, he recommended only debilitating agents in the treatment of disease. The English, Italian, and French systems had, during the first two or three decades of the nineteenth century, great influence in determining the use of drugs, and the doctrine of Broussais affected treatment until after the middle of that century. But with increasing knowledge of Chemistry, Physiology, and Pharmacology belief in the Brunonian and allied systems gradually declined.

The last conception of disease and its cure which I shall notice is that of Hahnemann, who, at the end of the eighteenth century, made the hypothesis that "like cures like" the central point of a new system of therapeutics. Hippocrates pointed out the occasional value of similars, that is, of drugs which produce symptoms similar to those observed in the disease for which they are given; so, too, did Galen, and some later writers. But Hahnemann was the first who raised the proposition that like cures like into a natural law; and he conjoined with this view a belief in the power of infinitesimal doses. He formulated new hypotheses to account for the disease and the curative action of his drugs. He held that a spiritual power (the vital force) animates the human body, and that disease consists in a diversion of the automatic vital force into an abnormal direction. Drugs rightly selected can produce, in his opinion, a disease like to, but stronger than that for which they are given, and such medicinal diseases are more easily overcome by the spiritual or vital force than natural diseases. In selecting a drug for any particular ailment, it is therefore necessary to choose one which produces symptoms like to those which are present in the natural disease for which it is given. He said that knowledge of pathology, or of the causation of disease, is useless. The powerful action of infinitesimal doses he attributed to the fact that in their preparation succussion and trituration were much used, and these processes in his belief increased enormously the spiritual or dynamic power of the drug. As he used mercury in some of his preparations, it is probable that the oxidation of metallic mercury and the conversion of the subsalts into the more powerful persalts by trituration were important truths as a basis for his dynamic hypothesis. Hahnemann's suppositions as to the nature of disease and drug action have long died out; but there are still a few believers in the so-called law of "similars" and in the efficacy of drugs given in infinitesimal doses.

With Brown, Broussais, and Hahnemann another phase in the history of drug treatment closed. With them the theoretical systems of treatment, which had succeeded one another since the sixteenth century, came to an end. Therapeutics became rational. A tendency in this direction had long been manifest; with the increasing knowledge of Chemistry, Anatomy, and Physiology during the seventeenth and eighteenth centuries, truer conceptions of the causes of diseases became more general; and it came to pass that drugs were increasingly used for the removal of causes apart from belief in any abstract generalisations.

Alkalis were given for acidity, even though chemical conceptions of disease were discarded. The knowledge that the bronchial tubes are surrounded by muscle led to the tentative administration in asthma of substances such as opium and ether, without relation to any hypotheses; and the good effects observed from evacuants in many ailments led to their extended use, without any definite regard to Sydenham's idea of aiding nature.

Morgagni's great work on *Pathological Anatomy*, published in 1795, threw a flood of light on the conditions of disease, and Bichat not only pointed out the importance of considering changes of tissues, as well as of organs, but urged that the true use of medicine is to restore organs and tissues to a normal state; and, by the discovery of the influence which drugs have on tissues and organs and the functions they subserve, the way was cleared for the next great step in therapeutic progress. The advances of chemistry gave facilities, previously wanting, for exact investigation of the action of drugs. Stoerk, indeed, in 1762, had published a good account of the action of henbane, aconite, and some other drugs on the healthy organism, together with the therapeutic inferences he drew from this action; we find, however, few records of similar investigations, and at the end of the eighteenth century very little had been ascertained as to the exact manner in which drugs influence the body, or as to those constituents of drugs on which their properties are now known to depend. The progress of chemistry had indeed led to a search for active principles in vegetable substances; but Cullen (in 1778) threw doubt on the value of any attempts to determine them. In the early part of the nineteenth century, however, chemists were enabled to separate several important alkaloids. Morphine was discovered in 1816, quinine in 1820, strychnine in 1818. These discoveries facilitated those investigations into the action of drugs on the various organs and tissues of the body and their functions, of which Magendie was the pioneer, and have so largely influenced the therapeutic hypotheses and practices of the present day. Magendie showed that it was possible to determine not only the organ on which a drug acts, but even the part of the organ. By a series of striking experiments he demonstrated that strychnine produces its tetanising effects not by influencing the nerves or muscles, but by acting on the reflex centres of the spinal cord; and the methods by which he showed this have been more or less a model for all who have forwarded the work which he so ably initiated. Soon chemists throughout Europe were busy in attempting to separate the active principles from all the well-known drugs; and physiologists were equally active in trying to determine exactly the organs on which these principles act, and the manner in which they affect them. Foremost among such workers was Claude Bernard, to whom, more than any man in that century, we are indebted for the progress made in the comprehension of the action of drugs; as, not only by his experiments on the physiological effects of many drugs, but also by his discovery of the part which the vasomotor nerves and the muscular coat of the arteries play in the circulatory

system, he prepared a way for the further investigations on the vascular system, which have led to the discovery of some of the most powerful means we possess for relieving suffering and saving life. His successors have been continuously occupied in following out the researches which Magendie initiated; and every year we see additions made to physiological and pharmacological knowledge, which, immediately or at some future time, will enable us to treat disease with increasing certainty. When it had been sufficiently demonstrated that substances derived from the mineral, vegetable, and animal kingdoms have a specific effect on disease, and that this action in the case of animal and vegetable substances could be traced to the chemical compounds they contain, the method in which the structure of these compounds influences their effects became a subject of investigation. Blake in 1842 came to the conclusion that all salts having the same base exert a similar action when introduced into the blood, and that a close relation exists between the chemical properties of substances and their physiological results.

We have now found that it is possible in many instances to form an idea, from the composition of a drug, of its influence on the body; that this influence may be altered in certain directions by modifying its chemical structure, and that new substances may be built up chemically to fulfil pharmacological and therapeutical requirements.

The advances of recent years have been chiefly in the direction of the discovery and production of new agents calculated to exercise definite pharmacological actions, of determining their exact influence, as well as that of the older drugs, on the various parts of the body and on the lower forms of life, of ascertaining the minute changes which take place in disease in the various organs, and of discovering the relations which exist between micro-organisms and the production of disease on the one hand and the products of the micro-organisms and the cure of disease on the other.

II. Present Principles of Drug Therapeutics

We give drugs in disease for two purposes:—

1. To restore health directly by removing the sum of the conditions which constitute disease. Here we act empirically, with no definite knowledge,—often indeed with little idea of the action of our drugs, but on the ground that in our hands, or in those of others, they have restored health in like cases.

2. To influence one or more of the several tissues and organs which are in an abnormal state, so as to restore them to or towards the normal, with the hope that if we succeed in our purpose recovery will take place. This purpose we effect by means of the influence which the chemical properties of drugs exert on the structure and functions of the several tissues and organs. Minute information, therefore, of the nature of the drugs and their action is essential for their proper employment.

Nature of Drugs.—Drugs were formerly looked upon as simple

substances having, amongst other attributes, the power of curing disease; indeed the popular idea concerning them has not advanced beyond this view; but physicians now refer their influence to the textural and functional changes they are capable of effecting in definite portions of the body by virtue of their total composition, or that of certain chemical substances they contain. Not only do the elements of which a drug is constituted affect its action, but the way in which these elements are grouped and combined is of importance.

The effect which several of the elements exert in their compounds has been traced by Binz, Lauder Brunton, Harnack, Richet, Dr. Ringer, and others. It has been shown that chlorine and bromine, potash, lime, and many other metals, always tend to act on certain tissues in a definite manner, unless their influence be neutralised by other elements with which they are in combination. It has been shown also that small groups of elements may play a similar part in more complex compounds, that the action of NH_2 and NO_2, for example, can be as distinctly traced in the compounds in which they occur as that of chlorine or potassium or calcium. A compound containing the group NH_2 stimulates the medulla; a drug containing the group NO_2 acts on the vessels and dilates them.

On the other hand, in many of the organic compounds we are quite unable to trace the effects of the several elements; and it is rather the manner of grouping of the elements which seems to confer on the compounds their pharmacological and other properties. Two compounds may contain exactly the same elements and the same number of atoms of each, yet if these atoms be differently arranged the compounds may differ entirely in pharmacological and other properties. Methyl nitrite, and nitro-methane have the same formula (CH_3 NO_2), but the oxygen and nitrogen atoms in the two substances are joined together in a different way. The result is they act quite differently: the nitrite dilates the vessels; nitro-methane has no such action.

In the more complex organic compounds the addition or removal of one of these small groups of elements often greatly alters the pharmacological effect. Professors Fraser and Crum-Brown showed many years ago that by replacing an atom of hydrogen in conine by one of methyl (CH_3) a great change in properties was effected. Conine paralyses the nerve-endings alone; the methyl compound depresses the spinal cord. It is not always possible to anticipate the influence which the addition or subtraction of one or more of these groups will have on complex compounds which, like the alkaloids, are made up of a very large number of simpler groups. The result doubtless depends on the place which the added group takes amongst the other groups, or the effect produced by the subtraction on the arrangement of the other groups. Though the character and arrangement of the groups in a compound do not certainly indicate the action, yet they often give a good clue to it; they point to the manner in which the compound breaks up when taken into the system, and suggest the new combinations which may be formed.

Again, they often indicate modifications and additions by which new compounds may be produced for the fulfilment of needs. Thus, for example, by adding the group NH_2HCO to the group CCl_3, COH (chloral) we get a compound chloralamide (CCl_3 CHO HCO NH_2) which has the soporific properties of chloral, but does not so deleteriously affect the cardiac and respiratory system. By the substitution in sulphonal of a molecule of ethyl (C_2H_5) for a molecule of methyl, trional is formed, which appears to have in some cases a better effect than sulphonal. Many of the modern remedies are the outcome of a knowledge of the influence exerted by various groups, and by the manner of arrangement of such groups in a compound.

In the laboratory we can easily so modify the composition of medicinal agents as to transform them into compounds having very different pharmacological effects.

If morphine (C_{17}, H_{18}, NO_2 (OH)) be boiled under pressure with water acidulated with hydrochloric acid, it loses a molecule of H_2O, and is converted into apomorphine (C_{17}, H_{17}, NO_2). If it be heated with soda and methyl iodide, codeine (C_{17}, H_{18}, NO_2, OCH_3) is formed. Pilocarpine, when heated with dilute hydrochloric acid, is converted into jaborine, a compound allied chemically to pilocarpine, but resembling atropine in its pharmacological effects.

The changes which can thus be effected in a drug outside the body may also be produced within the body; moreover, these changes may vary with the conditions of the body. It is important, therefore, to determine the changes which can occur in chemical compounds under varying circumstances.

In drugs derived from the mineral kingdom the grouping of the elements is simple; the influence of the drug often depends almost entirely on one of the elements present—as, for example, in the compounds of iron and mercury—and we can easily comprehend all the possible alterations which such drugs may undergo in the system.

In the case of organic compounds belonging to the fatty and aromatic series, again, we may sometimes trace out the nature of the decomposition which goes on in the body, and estimate the effect of any new compounds which may be formed; but when we administer very complex substances, like the alkaloids, it is often impossible in the present state of knowledge to determine what changes, if any, take place; we cannot know, therefore, the nature of the effects which may be produced.

Still more difficult is it to determine definitely the action of crude vegetable drugs, the effects of which are due to the alkaloids, glucosides, oils, etc., which they contain. In many instances more than one of these active principles are present, and not unfrequently we find these closely related chemically, being probably derived one from another in the chemical processes going on in the plant.

The number of active principles in a plant is largely influenced by the circumstances connected with its growth, such as temperature, nature of soil, and so forth. Stenhouse found that broom grown in the sun

contains four times as much alkaloid as that grown in the shade. Not only so, but the relative amounts of the various active principles will vary somewhat as the conditions under which the plant is grown are favourable to the occurrence of chemical changes, or the reverse.

From all these causes the effects of crude vegetable drugs, and therefore of the galenical preparations obtained from them, are apt to vary; and this variation is at times increased by differences in the method of preparation. Hence arises, perhaps, the divergence of opinions so often noted with regard to the therapeutic powers of certain drugs. The process of "standardisation" which has been already adopted in twenty instances in the British Pharmacopœia will to a certain extent obviate this source of error; for the standardised preparations will contain a uniform amount of the alkaloidal principles contained in a plant. But if the relative quantities of these principles vary under different conditions of growth, the effects of preparations apparently identical will still be liable to corresponding variation; this may occur especially where drugs contain substances easily modified, as in the case of atropine and hyoscyamine. Ladenberg has given reasons for believing that the latter is changed into the former even by the process of extracting the alkaloid. Examples of such readiness to change, however, must be rare.

Notwithstanding all these possible sources of error the action of drugs on the system is moderately constant; but not until we are much better acquainted than we now are with the chemical nature of drugs shall we be able to explain the very diverse therapeutic results which are recorded.

The Nature of Pharmacological Action.—By the word "pharmacological action" is meant the action of remedial agents on tissues and the function they subserve in health and disease.[1]

The ultimate nature of the influence which drugs exercise on organised material cannot be absolutely determined; but, as Schmiedeberg has said, it must be chemical—using the word chemical in a broad sense.

When a pharmacological agent comes in contact with a tissue its effects may be purely chemical; it may act in virtue of its acid or alkaline properties, or by leading to decomposition of a purely chemical nature. It may also effect changes in the tissues by coagulating the albuminous or gelatinous materials contained in them; but, beyond this, it may alter their functions and vitality, without, so far as we can tell, producing chemical change in the strict sense of the term. When, for example, we pass through the muscle of a frog a very dilute solution of barium

[1] The word "pharmacology" was formerly applied to the consideration of medicines generally, including their physical characteristics and mode of preparation: and in this sense it is still often used in other countries. In England it signifies that department of therapeutics which concerns the effect of remedies as distinguished from their therapeutic application. It is well that the term "pharmacology" should be taken as including the action of drugs on morbid as well as on healthy tissues; otherwise it would be synonymous with physiological action, and we should have no term applicable to the investigations of the action of drugs on morbid tissues.

chloride, or expose it to a similar solution, the function of the muscle is distinctly modified, as shown by its increased contraction to stimuli, and by the prolonged duration of the contraction. By acting on the muscle of the heart or the vessel walls, their functions and vitality may also be altered; the systole of the heart is strengthened and prolonged, and the vessel walls are contracted. But if, after producing these effects on voluntary muscle, heart or vessel, we take means to wash the tissues through with a nutrient fluid containing no poison, the muscles and organs will resume their normal functions. We can, moreover, antagonise the effect of chloride of barium by means of a weak solution of potash, or by a solution containing NO_2, combined with a comparatively inactive base (sodium). In the latter case, however, NO_2, though neutralising the modification effected by barium on the function of the muscle, joins with it in depressing vitality, and the muscle quickly dies. A minute quantity of calcium chloride, on the other hand, whilst affecting the contractility of muscle, tends to prolong vitality. Now in these cases there is no evidence that any chemical change takes place; the influence is apparently molecular rather than chemical, for if positive chemical change took place it is not probable that the effects could be so easily abolished, either by the removal of the barium, or by the addition of substances between which and the barium chloride no chemical change takes place. The exact process by which the molecule of the drug acts on the ultimate elements of the muscle-fibre in order to produce change in function is beyond our knowledge. It seems probable that the influence of chemical compounds on the muscular, nervous, and all other tissues of the body, is similar to that which occurs in the skeletal muscles or heart removed from the body. The functions of the tissues are altered by the influence which the molecules of the chemical compounds exert upon them, and their vitality raised or depressed. It is in this way that strychnine and physostigmine respectively stimulate and depress the spinal cord, that curare paralyses the nerve-endings, that atropine paralyses the vagus endings and centre, and that the tissues engaged in secretion or excretion are stimulated or depressed. Most substances at first increase and then decrease the functional activity of muscle; in some the stimulating, in others the depressing effect is more marked: in some substances, indeed, no primary stimulating effect is observed. The same is the case with regard to the action of drugs on the other tissues within the body. Remedial agents for the most part first stimulate and then depress the functional activity of the parts they influence; but the stimulation may be more marked than the depressing effect, or *vice versa*; or it may be entirely absent.

The effect in all cases may be looked upon as "molecular," that is, it may be produced without ascertainable chemical or structural change. If the supply of the chemical compound in the blood cease, it is sooner or later washed out of the tissue by the circulating fluid, and the normal function is restored. In experiments on muscle-tissue it can be shown that some substances, such as the nitrites which powerfully alter func-

tional activity and vitality, can be easily washed out, and the muscle thus restored to its normal condition. Other substances, such as barium, are washed out with difficulty. It is probable that there is a similar difference in the influence of drugs on all tissues, and that this in part accounts for the well-known difference in the duration of the action of medicines. The removal of a drug from the tissues which it has temporarily influenced, unless the effect have been very strong, is followed by a return to the normal state; but it seems probable that under some conditions the continued interference with the function of a part is followed by nutritional changes of a permanent character. It is from this cause probably that alcohol in time leads to those changes in muscle and nerve which are characteristic of its prolonged imbibition.

In order that drugs taken by the mouth may act on various parts of the body, such as the spinal cord, brain, and nerve-endings, it is evident they must be absorbed and carried by the blood to these several parts. The absorption of active principles no one now questions, though in earlier days it was denied. Cullen held that medicines act almost entirely by the influence they exert on the mucous membrane of the stomach and intestines; and in the first decades of the last century the necessity for the absorption of a drug antecedent to its action was doubted by many. Drugs carried by the blood do not affect the tissues equally: one exercises its influence on the tissues of the cord, another on those of the cerebrum, a third on the respiratory centre, and so on. To explain this we must assume that tissues have a selective affinity, and that, as the blood circulates through them, each retains or submits to the material which is in functional relation to itself.

Perhaps the most difficult part of pharmacological action to determine is the influence of remedial agents on the blood and nutritional processes. There can be no doubt that some agents markedly affect the hæmoglobin in the corpuscles, as shown by the cyanosis they produce; others, like potassium chlorate, are under certain conditions capable of causing dissolution of corpuscles, and there can be little doubt that the alkalinity of the plasma may be increased or decreased. But over and above these effects it would seem as if some substances, such as alcohol and arsenic, are capable of modifying the metabolic changes—delaying or accelerating them; but whether such results are due to a primary alteration in the blood, or to a direct influence of the alcoholic or arsenical molecule on the tissues, is not known.

Besides influencing the functions of tissues in the manner which has been distinguished as molecular, drugs may produce direct structural changes in tissues. Apart from all chemical action, they may excite irritation and inflammation such as that which is produced by mechanical agencies. In this way they may produce important effects not only on the tissues with which they come in contact, but also on parts remote from them. By the irritation produced in the nerve-endings in the tissue a centre with which these nerves are connected may be altered, and other tissues supplied by this centre may have their function and

vitality increased or decreased. The vomiting produced by emetics, and the nutritional changes which occasionally seem to follow external applications, may be thus explained.

The influence of pharmacological agents under the abnormal conditions present in disease is by no means always the same as in health; the difference is, however, usually quantitative rather than qualitative. A weak-walled heart, for example, is much more easily influenced by digitalis than a healthy one. The functions of the kidney can never be affected in health as at times they may be in certain diseases. Antipyretics exert, on those parts upon which they act, a different effect in a febrile as compared with a normal condition. Lastly, mercury and iodide of potassium have special actions on certain forms of diseased tissue which we do not see in health. This is probably due to the fact that in the diseased conditions they act upon new tissues of a less stable character than normal tissue; or it may be that new compounds are formed with the mercury or iodide which are easily broken up and destroyed.

As already pointed out, the pharmacological action of a drug is apt to be influenced by changes which the chemical processes of the body effect in the drug itself. Such changes may occur in the gastro-intestinal canal, in the blood, in the tissues, or at the moment of excretion. Hence the chemical composition of a drug is not unfrequently the key to its pharmacological action.

Principles on which Drugs are selected.—*Rational Therapeutics.*—When a case of disease presents itself for treatment the first step is to determine whether any drug be known which has cured an exactly similar case. This can only be done, of course, when full knowledge of the clinical features and pathology of the case has been obtained. If no such drug is known, one of two plans is adopted: we may select a remedy on the ground of analogy, because it has done good in an instance so like the present one that it may reasonably be expected to be of service again. If experience and analogy fail, recourse must be had to such pharmacological knowledge as we may possess; that is, we may select a drug capable, directly or indirectly, of causing the return of one of the abnormal tissues and organs to a normal state.

Whether a drug be selected in the first place on analogical or on pharmacological grounds will largely depend on the bent of the observer. Some see analogies quickly, others more readily resort to reasoning. The same treatment may result from either attitude of mind.

The chief point in which the modern method of selecting a drug differs from that formerly employed is, that when empirical knowledge does not appear available we employ methods of reasoning founded more directly on the pathology of the disease and on drug action, instead of on metaphysical or fanciful views as to the nature of disease and of remedies. Nevertheless, it must be pointed out that in the application of pharmacological knowledge to the cure of disease we still use hypotheses; and on the correctness of these our results must depend. The pathological changes in every ailment are more or less complex and

widespread; the immediate influence of remedial agents is more limited: hence when we desire to restore health by urging the tissues and organs towards the normal state, we have to make choice of the pathological condition which shall first be dealt with; and this we do in accordance with certain imperfect inductions to which experience has led us. We assume in each case either (1) that in diseased conditions there is naturally a return to health, or (2) that if the apparent cause of the ailment be removed cure will follow, or (3) that by the restoration of tissues and organs, which are the special seat of pathological changes, to their normal textural and functional state, or to a state approaching the normal, we promote cure; and further, that when organs are caused by drugs to resume their normal function, their improved condition may continue even after the drug is withdrawn.

The first assumption is one on which Hippocrates and Sydenham relied, and it lies at the root of much of our therapeutic reasoning. Experience proves to us that many diseases tend to terminate in recovery; but that, nevertheless, pathological changes at times occur in their course which, unless prevented by suitable remedies, will terminate life. Yet we often fail to save life by dealing with sudden causes of danger. The removal of the apparent cause, or of the more marked pathological conditions in a disease, does not always lead to a favourable termination. Each of these generalisations, however, holds good in a large number of cases; and in selecting a drug apart from the teachings of experience we found our judgment on our pathological and clinical knowledge; we decide under which of these generalisations the case before us falls, and then with the aid of pharmacological knowledge we select a drug to fulfil one of the following indications—a drug which will (*a*) so influence some organ or organs as to avert the tendency to death, (*b*) remove the apparent cause of the ailment, (*c*) restore as far as possible the tissues and organs, which are the special seat of pathological changes, to a normal state. In addition to these indications we are manifestly called upon to (*d*) relieve pain and suffering.

Our success will depend on the correctness of our judgment as to whether the case really comes under the generalisation we employ, and on the correctness of our pharmacological knowledge.

It is apparent that in one sense indication *c* includes *a* and *b*. In averting death or removing the apparent cause, however, we do not necessarily deal with the special seat of pathological change. We always meet indication *a* at once, and then indication *b* if we can.

Experience and Analogy.—The cases in which experience founded on simple observation can be trusted in the selection of a drug are few. The same collocation of symptoms and conditions is rarely repeated; yet, unless it is, when we select a drug on the ground that it has before done good, we act on analogy rather than on actual experience. In times past the judgments formed on the ground of experience of the action of medicines were very fallacious; to this the enormous number of medicines then used and now discarded bears witness. Yet the

discovery of mercury, quinine, arsenic, and many other remedies is an evidence of the value of simple observation. Want of knowledge of the natural history of disease, of pathology, and of pharmacology is the cause of the errors which are made when experience is trusted alone.

Belief in a drug of no value is easily engendered if the natural course of disease be unknown; defective pathological knowledge and observation lead rather to the misapplication of useful remedies. Quinine rarely fails in ague; but in a counterfeit of ague, say in the intermittent hepatic fever due to gall-stones, it is useless.

Pharmacological knowledge corrects many of the errors to which simple experience is apt to lead; the want of it permits their continuance. If a drug have no active properties it is surely devoid of medicinal effect, unless it be a food; for medicinal action is the outcome of the effects of active principles on tissues. It is always possible that in any particular drug the active medicinal agent may have escaped notice; but in the present state of chemical science it is not likely that undiscovered principles reside in such substances as sarsaparilla and hemidesmus: yet these drugs are given on the testimony of experience,—a testimony no stronger than that which has supported scores of other agents eventually discarded. If the indications given by the pharmacological examination of a drug are opposed to experience in its favour, the latter must almost certainly be at fault.

Experience and analogy, then, should only be trusted within narrow limits; but when we can combine the indications of experience with those of pharmacology we strengthen both. The influence, for example, of antimony in eczema, especially when combined with magnesium sulphate, has often been vouched for on the ground of experience; but not more strongly than has been the case with scores of useless agents. It can be shown, however, that antimony does, in the frog, influence the epithelium very markedly, as does arsenic; and this, without proving its remedial value, distinctly adds to the probability that those observers are right who hold antimony to be useful in some forms of eczema.

The value of the antitoxins and of thyroid extract is vouched for by many careful observers. Pharmacological knowledge is certainly not opposed to the probability of their usefulness; it rather supports it. On the other hand, it has so far given no support to a number of new animal substances brought forward recently, many of them on analogical grounds founded on some error in observation. To the use of analogy in drug therapeutics we owe great advances, especially in early times—it has been a great inciter to experiment, and is so still. Guided by due knowledge of the course of disease and of pathology it leads to increased knowledge; but as used in times past it has burdened our Materia Medica with much rubbish, inasmuch as recoveries following the use of substances suggested by analogy have been looked upon as cures. It was by false analogy that mercury came so much into use in inflammations. When mercury was found to influence so markedly the swellings and thickening occurring in syphilis, it was used by analogy in all the forms of inflammatory

disease which cause swellings and thickenings. As many of these naturally subsided thereafter, mercury was thus credited with a curative power in inflammation. It would be going too far to say mercury has no influence in inflammatory changes. There are probably conditions in which it is of service, but the facts that it is now so little used, and that no apparent evil has followed its abandonment, indicate that the views formerly held, and apparently grounded on experience, were, to a large extent, erroneous; and that the employment of analogy may, in this instance, have been productive of evil.

(*a*) *Method of averting the Tendency to Death.*—We find not unfrequently in the progress of acute diseases, and sometimes in other circumstances, that death seems to be impending by the failure in function of one organ when the condition of the others is compatible with continued life; and this even when in the organ affected there is no evidence of fatal structural change.

The cardiac and respiratory systems are most commonly those in which such failure takes place. Suddenly or gradually, during the course of many diseases, the condition of the pulse points to failing heart action which threatens life; or again the blood changes essential to the continuance of life are imperilled by failing powers of the respiratory centre, or by paroxysmal obstruction to the entrance of air into the lung. These events may happen even though the heart and lungs are not the seat of any considerable pathological changes.

In case of heart failure we may fulfil the indication of averting the tendency to death by giving drugs which (i.) strengthen the power of the heart or (ii.) decrease the work it has to do.

(i.) In selecting drugs to strengthen the heart the whole of their pharmacological properties must be borne in mind. Digitalis is one of the most effective agents we have for increasing the power of the heart's action, but it contracts the vessels and is long in acting. By contracting the vessels it is capable of doing harm in certain cases of heart failure, especially in gouty people with tendency to high arterial pressure; and because of the slowness of its action (especially when taken by the mouth) it is often given in vain in cases where the heart's failure is urgent. On the other hand, where the heart's failure is gradual and the arterial pressure low, digitalis is called for. Strophanthus does not contract the vessels, and seems to act more quickly; whether it acts as powerfully as digitalis, is a point on which we are not agreed. Strychnine, as a heart stimulant, acts more rapidly than digitalis; when given subcutaneously its effects can often be noted in a few minutes; and, though perhaps they do not last so long as those of digitalis or strophanthus, they are more permanent than those of the volatile cardiac stimulants. Strychnine, moreover, has the advantage of being a respiratory as well as a cardiac stimulant: ammonia shares this advantage with strychnine, but it is more evanescent in its influence on the heart, although perhaps more immediate in its effects. The injection of ether subcutaneously is the most powerful means we have of immediately

stimulating a failing heart, but its action is probably even more transitory than that of ammonia; though, owing to the fact that it can be injected subcutaneously, it is more frequently employed in urgent depression of the heart's power. The cardiac stimulation produced by smelling ammonia is of course of a reflex nature. Although ammonia has undoubtedly a stimulating effect on the heart, increasing both its force and frequency, it is not always easy to determine its utility in this direction. It is possible the condition of the stomach at the moment influences its cardiac effects to some extent. So far as it is converted into chloride it can have little action on the heart, although the chloride may stimulate the respiratory centre.

(ii.) Of drugs which act by dilating the vessels, and thus relieving the heart in its work, there is one—amyl nitrite—which dilates the vessels in about ten seconds, and is therefore applicable in the most urgent cases. As its influence on the circulation, however, ceases in two or three minutes, this drug, though of great value in immediate exigencies, must not be relied on for continuous action.

Nitrite of sodium and nitro-glycerin exert a distinct influence in from two to four minutes, but their effects continue for two or three hours; they are therefore serviceable in cases where we want to relieve the heart's action for a considerable period, though useless where instant effect is required.

Vessel dilators are of special use in warding off evil where cardiac failure is not accompanied by vascular dilatation. In certain forms of cardiac degeneration it would appear as if periodic waves of increasing arterial contraction become a grave source of danger, and these may be well met by the quickly or by the more slowly acting vessel dilators according to circumstances.

It is possible in some cases to combine a cardiac stimulant with a vessel dilator; indeed, the vessel dilators may have at first a slight stimulating effect on the heart, even if, in large doses, they eventually depress it, which, however, is not definitely proved. The combination of a nitrite with ether is thus often distinctly advantageous in the relief of cardiac failure.

Any lethal tendencies of drugs used in cases where life is in the balance must always be borne in mind. It can be shown by experiments on animals that a slight excess of digitalis over the amount required to stimulate the heart may cause an immediate and permanent cessation of the beat; and there is reason to believe that in some forms of cardiac degeneration digitalis is capable of stopping the heart's action suddenly. On the other hand, in certain other ailments, such as pneumonia and delirium tremens, it would appear that the heart can bear large quantities of digitalis without injury. Unlike digitalis, strychnine seems to have no lethal effect on the heart even when given in large medicinal doses; and we rarely see indications of the physiological effects of strychnine on the nervous system following their use. The powerful effects of the nitrites on the circulation make us cautious in the use of these agents, the more so

since, as before said, they are capable of depressing the contractile power of the heart: it is worthy of note, however, that, considering the extent to which they have been used, grave evil has very rarely been attributed to them; this may be due to the fact that the molecular influence they exert on tissue is not so permanent as in the case of many other drugs. It has been shown that they can readily be washed out of muscle-tissue, which then resumes its normal function.

In cases where life is immediately threatened by defective blood changes due to failure of the respiratory centre, or to paroxysmal obstruction to the entrance of air into the lung, we may in the first place administer substances which have a directly stimulant action on the respiratory centre: of these perhaps the most useful are ammonia and strychnine.

Belladonna has also a powerful effect on the centre; it has an influence, too, in relaxing undue contraction of the muscles of the bronchial tubes if it occur. In using it, however, we must bear in mind its wide influence over many other systems of the body.

In paroxysmal obstruction to the entrance of air into the lung the nitrites will often be found of value; one or two drops of liquor trinitrini, or a drachm of a 3 per cent solution of nitrite of ethyl, or two grains of sodium nitrite, will very often remove perilous dyspnœa by relieving the spasm which interferes with the entrance of air into the bronchi.

Even when we cannot remove the causes which lead to defective aeration of the blood, we may sometimes temporarily neutralise their ill effects by the inhalation of oxygen. It is quite true that in most cases where oxygen is used no permanent good is effected; but it is very commonly employed where the causes which lead to defective aeration are continuous: as a means of removing temporary cyanotic conditions oxygen is distinctly useful.

The reduction of hyperpyrexia occurring in the course of acute diseases is another instance of the use of drugs in warding off a tendency to death; but here drugs are probably of less value than other means. If drugs are employed, quinine is by far the best remedy for this purpose, but less than 10 grains is generally useless. The employment of antipyrin, antifebrin, or phenacetin is very questionable practice.

(*b*) *Removal of the apparent Cause of the Ailment.*—In the removal of remote causes of disease drug treatment takes but little part. A foreign body in the stomach or intestines may be the cause of the pathological conditions leading to colic, vomiting, or diarrhœa; and we employ pharmacological knowledge in the selection of emetics or purgatives for their removal.

Micro-organisms, too, may be looked upon as the cause of a large number of ailments. Proof is yet wanting that we can destroy micro-organisms in the blood and tissues by so-called germicidal substances such as perchloride of mercury, the sulphites, carbolic acid, etc.; even on external surfaces and on mucous membranes, as in ringworm and diphtheria, these substances often fail to destroy them, though they are capable of checking their growth.

Most of the other conditions usually called "causes" of ailments are really abnormal conditions of tissues and organs giving rise to groups of symptoms. In the series of antecedents which constitute collectively the true cause of an ailment, we often stop in an arbitrary manner at one of them and call it the cause of the collocation of phenomena by which the disease is signified. Practically by the word cause is usually meant the most remote of the antecedents which it is in our power to influence by drugs; it is by no means always the most manifest.

In considering whether it be possible to remove an apparent cause we have first to decide whether it is really in action, next whether it goes far enough back in the chain of antecedents, and, lastly, how far drugs can influence it. A gumma may have been the direct cause of a hemiplegia; we may remove the cell-deposit by mercury and iodide, but yet no improvement may take place, for further structural changes have occurred. The gumma may not still be the cause of the loss of power, although at first it was. Again, cerebral symptoms may be due to changes in the vessel walls and high arterial pressure—the latter being the outcome of the products of imperfect metabolism, which in their turn may have originated in imperfect digestion. To treat the high tension will not suffice: it does not go far enough back in the order of events: we must treat the imperfect metabolism or the indigestion. Lastly, the limit of the action of drugs comes to be considered: in the case of gout, syphilis, and a few other ailments we can definitely affect structural change by drugs; in most cases, however, our power to remove a cause by drugs ceases as soon as it consists of definite statical tissue-change.

The indication to remove the cause might of course be included in the next one relating to the removal or diminution of the special pathological changes present; yet practically in selecting a drug we have always first in our mind this question of cause, and it often leads to the selection of an apparently subordinate lesion for treatment. In nothing is the judgment more exercised than in determining whether we shall deal with the remoter or with the more immediate or evident causes of the case before us. After all, however, the removal of a remote cause, like the removal of the immediate factors threatening death, is only an instance of the general statement that when empirical treatment fails or is not possible, we try to cure by restoring individual organs as far as possible to a normal condition.

(c) *Restoration of Tissues and Organs which are the Seat of Special Pathological Changes.*—The influence of drugs in restoring organs to their normal state depends, of course, on the tissue-changes they are capable of effecting—using the word tissue-changes in its widest sense to indicate changes which we cannot physically determine, as well as those we can. This tissue-change, again, is the outcome of the action of elements or groups of elements in a drug on one or more areas of the body.

The general methods adopted when the blood is in an abnormal state may be mentioned first. In some cases we have evidence that the normal

constituents of this fluid are defective; in others we have reason to believe that substances not ordinarily contained in it are present; or that some of the normal constituents may be present in excess. In the first place we may attempt directly to make up the deficiency. We do this when we give iron in anæmia; for recent evidence does not tend to support the views of Schmiedeberg and some other observers, who have asserted that in the use of iron nothing is added to the blood, and that its effects are due to changes brought about by it in the intestines. Another example of adding a constituent wanting in the blood is seen in the administration of the thyroid gland; while bone-marrow acts like iron, if, indeed, it have any effect at all. To remove abnormal substances present in the blood various means are adopted. If we have reason to suppose that the products of imperfect metabolism are present, we may attempt to promote their excretion by the kidneys or bowels. It is possible, though by no means proved, that such products are excreted by the bowels; it seems likely that saline diuretics may also help to remove them. Another and often a more effective plan is to prevent absorption of the contents of the intestine in the upper part of the intestinal canal by means of saline purgatives, such as sulphate of soda and sulphate of magnesium; a third is to give drugs which are supposed to facilitate the burning up of the intermediate products of metabolism. Alkalis, for example, are sometimes used for this purpose.

There seems reason to think it possible in certain cases directly to antagonise and destroy the effects of some toxic matters which cause disease. This at least seems the way in which the antitoxins act. It is supposed, for example, that the diphtheria and tetanus antitoxins act directly on the toxins, annulling their noxious influence. May it not be, too, that quinine, and likewise mercury, respectively antagonise the poison of the parasite in ague and the toxic agent which exists in the blood in syphilis?

The chief effects of disease on other tissues and their functions which may be influenced by drugs are connected with—(α) Inflammation and its results. (β) Other morbid processes which lead to cell-growths. (γ) Increased or defective function with or without ascertained physical changes.

Though inflammation may be, on the whole, a protective process—the reaction against some injurious material, as Metchnikoff thinks—yet, as he also points out, its local effect on tissues essential to life may be destructive [*vide* art. "Inflammation"]; drugs are therefore used to mitigate or limit it. External inflammations may be dealt with by local stimulants or local sedatives. In conjunctivitis, for example, very dilute solutions of zinc sulphate are applied to the inflamed surface, and manifestly tend to subdue the process. They are supposed to act by contracting the dilated vessels. It would seem at times as if substances such as atropine and morphine, which depress the functions of the sensitive nerve-endings in tissues, have a beneficial effect in relieving external inflammation.

Inflammatory processes in the gastro-intestinal canal may be affected in a similar manner. It seems probable that minute doses of irritants, such as ipecacuanha and iodine, may sometimes act in the stomach and intestines as very dilute solutions of sulphate of zinc act on an inflammed conjunctiva.

Furthermore, in the stomach and intestine we may affect inflammatory tissue favourably by altering its surroundings, by removing irritating material from the surface of the inflamed membrane, and perhaps by supplying an unirritating covering in the shape of bismuth. This supposition, however, to account for the good effects which bismuth undoubtedly produces in irritated conditions of the stomach and intestine is very doubtful. It is at least as probable that an extremely small amount of the bismuth, in contact with the mucous membrane, becomes decomposed, so that some soluble bismuth is formed, which, being a tissue irritant, acts as the zinc sulphate does on the conjunctiva. All inflammation of parts which can be reached directly by local applications are amenable to similar treatment. We can act, for example, on the inflamed mucous membrane of the bladder by sedatives, or by slightly stimulating and germicidal substances which are taken into the mouth, carried by the blood to the kidney, and there excreted, as, for example, buchu and copaiba. It is quite possible, too, that we may be able to influence the lining membrane of the tubes of an inflamed kidney, but definite proof that we can do so with advantage has not yet been given. In cases where there is invasion of the kidney by microbes we can render the urine aseptic from the tubules onwards by the administration of hexamethylenetetramine (urotropin), which during its secretion acts as an antiseptic. It must be borne in mind that the whole surface of the gastro-intestinal mucous membrane, from the fauces downwards, acts to some extent as an excreting surface; so that we may influence inflammatory processes therein by the excretion of substances previously absorbed. There is some reason to believe, for example, that the advantages of chlorate of potash in inflammation of the fauces are connected with its excretion by the mucous membrane, and are not entirely due to its local influence at the time it is swallowed.

What power have we of affecting inflammation of organs which cannot be reached directly, or through the processes of excretion? It was formerly held that in antimony, aconite, and calomel we have substances which directly limit the inflammatory processes in tissues; but no proof of this has ever been brought forward, and the belief is waning. It is probable that we have some power to act indirectly on inflammatory processes in the internal organs. We can increase secretion in the neighbourhood of an inflamed part, and we can alter the general tension of the vascular system. We can also modify the local vascular condition to a slight extent by dilating vessels in parts adjacent by means of pharmacological agents. In two other ways, also, it is possible by drugs indirectly to influence inflammatory processes in parts subjacent to cutaneous surfaces. There is evidence that cutaneous irritation has a distinct effect on

the vascular supply and the nutrition in adjacent parts, and clinically it appears in some cases to limit inflammation. The other method is to give drugs which exercise a sedative influence on the mechanical conditions affecting the part inflamed. It is thus that opium is used in peritonitis.

The products of ordinary inflammation which interfere with the functions of tissues may possibly, when consisting of cell-growths, be broken up and absorbed under the influence of mercury and iodide of potassium, as the products of syphilitic inflammation certainly are. We have as yet no strong proof of this, though analogy has led to an extensive use of both substances for the removal of the various forms of inflammation; and the disappearance of exudation has so frequently followed the use of these drugs that we can hardly doubt that some useful effect is produced. There is reason to believe also that we can cause the absorption of inflammatory exudations by stimulating the nerve-endings in adjacent areas. As a rule, for this purpose, preparations containing mercury or iodine are employed, often with friction. It is a moot point whether the dissipation of inflammatory exudations which certainly appears to take place under these applications is due directly to the absorption of these substances, or indirectly to their stimulating action on the cutaneous surface. Though mercury will pass through the skin, we have no proof that either iodide of potassium or iodide of lead do so: nevertheless they are manifestly of service at times. On the other hand, the irritation they cause is so slight that we can hardly attribute to this agency the absorptive influence these applications seem to possess.

Concerning the removal of other cell-growths which interfere with the functions of tissues we have but little information. In all ailments which have any resemblance to the syphilitic granulation tissue-tumours we use mercury and iodine, and not unfrequently we see absorption take place; but we do not at present know the natural history of such ailments sufficiently well to feel assured that the disappearance is due to the drug. Arsenic can be shown to have a very decided effect on the nutrition of the skin, and it sometimes distinctly influences inflammatory deposits therein. It is supposed also to exert some influence on sarcomatous and carcinomatous tissues, but here again more exact observation is required.

Drugs such as chloral, belladonna, physostigma, and nux vomica act on the tissues of certain parts of the brain and spinal cord, and thereby increase or decrease the functions of those parts. We can depress the functions of the motor nerve-endings with conine, and the sensory nerve-endings with aconite. We can paralyse the involuntary muscle-fibres directly with the nitrites, or indirectly by chloral hydrate, which depresses the functions of the vasomotor centre. We can stimulate or depress the functions of the cardiac muscle. The tissues of the various glands may likewise be stimulated or depressed. We can improve the nutrition, and therefore the function, of almost all the tissues by iron, cod-liver oil, and lime; and indirectly we can produce the same effect by

the gastric tonics and digestives which promote the taking and absorption of food.

Our knowledge of the method in which drugs' influence tissues in health and disease is largely, of course, the outcome of observations made on the effects of drugs on the functions which they modify; we must discriminate, however, between the action of drugs on an organ as a whole, and the changes in function which arise from drug influence on one of its tissues or on one of its parts. In restoring the function of an organ we have then to consider the influence of the drug on the various tissues and parts of which it is composed. In dealing with the cerebral functions, for example, the effect of the remedy on vessels as well as on cerebral tissues must be remembered; and in the restoration of the cardiac functions the effect of agents on various portions of the nervous system as well as on the muscle should be borne in mind. The influence, too, of changes in one organ on the functions of another are very considerable, and it is often by acting on a healthy organ by stimulating or depressing its functions that we are able to restore another from a pathological to the normal condition.

In a case of cerebral hæmorrhage, for example, in which the brain is the main seat of pathological change, we know of no drugs which by directly influencing its tissues will bring about its return to a normal state. We are able, however, to act upon it indirectly by purgatives which tend to lower blood-pressure, and after a while by giving drugs which improve the general nutrition. In valvular affections of the heart we cannot remove the chief pathological condition, but by acting on the cardiac muscle and its ganglia we can so strengthen and moderate the beat as practically to restore its normal function.

In phthisis we have hardly any power to influence lung-tissue directly: but, by substances such as cod-liver oil and lime, which improve the general nutrition of the body, we can indirectly, perhaps indeed to some extent directly, help to restore the lung-tissue and function. In bronchitis we can act directly on the tissue of the mucous membrane, and promote its normal secretions; but in pneumonia we probably cannot influence the affected tissues directly, although we employ salines with a vague idea that we may do so. Here we are limited in our action to sustaining the functions of other parts, in which the pathological change is much less marked, until such time as resolution may take place. It is possible, indeed, that expectorants sometimes influence the lung changes favourably by promoting secretion from the bronchial mucous membrane adjacent to the inflamed tissue; but it is unlikely that they act on this tissue itself. In pleurisy we are quite as helpless so far as direct drug treatment is concerned; we know no drug which has any direct effect in reducing pleural inflammation, and we are limited for the most part to the use of agents for the relief of pain. Yet even here, when the acute stage has passed, we may promote the restoration of the pleura to a normal state by iron and nutrients.

Though we have no more power over peritoneal inflammation than

we have over that occurring in the lungs or pleuræ, we are able in peritonitis to give some aid by limiting the movements of the inflamed part. Opium probably influences the nerves supplying the intestinal muscles, and thus decreases peristaltic action. It also fulfils the next indication, the relief of pain. Here again, as in many other instances, in the efforts we make to restore parts pathologically affected we act on other and more or less normal structures. We have no reason to believe that the chief effect of opium, either in relieving pain or in checking peristalsis, is due to any large extent to its action on the nerve-endings in the affected part.

In a few cases we attempt to restore the normal functions of an organ by the addition of certain materials which are lacking in its secretion. Thus, for example, in dyspepsia we administer pepsin; or we may aid duodenal digestion by a remedy derived from the pancreas; or we may give bile where we think this secretion defective. In all these cases, however, our immediate objects are in the first place to relieve discomfort, and in the second to restore the normal functions of the gastro-intestinal tract which are interfered with by the abnormal state of their contents due to the absence of pepsin, trypsin, and bile.

Sometimes we appear to apply pharmacological substances to influence a symptom rather than a pathological state, as when we use an antipyretic in fever. Here, however, we are really attempting to act on the pathological conditions causing high temperature; but not knowing what these are, we have to use a remedy in ignorance of the exact nature of its action.

In administering drugs to restore tissues and organs to a normal state we usually act on the supposition that an organ thus restored will maintain its improved condition even when the drug is withdrawn. When digitalis, for example, is given in cardiac dilatation and irregular action it is assumed, and for the most part rightly so, that if we can restore or partially restore the heart to a normal state it will so remain when the medicine is withheld. We do the same in bronchitis when we administer expectorants; in fact we apply a generalisation in this matter, as in many others, founded on a weak induction which must be referred to one or more inductions of wider scope. The reason that a tissue or organ restored to its normal state by a drug does not revert to its abnormal condition on the loss of the drug is partly that every altered condition of an organ reacts on the surrounding tissues and organs; and partly the tendency to revert towards the normal when perturbations have ceased to act.

(*d*) *Relief of Pain and Suffering.*—This indication has to be followed not only from considerations of humanity, but because pain and suffering, by their influence on nutritional processes, tend directly to prevent the return of tissues and organs to their normal state. The relief of pain may be accomplished by drugs which depress the functions of the sensory nerve-endings, or act on certain parts of the central nervous system.

The nerve-endings may be affected through the circulation or directly. It is probable that most of those substances which depress the tissues of the central nervous system, those especially which are in relation to its higher functions, have also some influence on the nerve-endings, though by no means in like proportion. On the other hand, substances, such as cocaine, which very distinctly paralyse the sensory nerve-endings have comparatively little effect in preventing the perception of pain in the cerebrum. The influence of substances which act directly on nerve-endings is practically much affected by the relations between themselves and the epidermis. The epidermic covering is probably a complete bar to the action of cocaine on the nerve-endings; proof has not yet been given that, even by combining it with substances such as chloroform and lanolin, which are said to aid the passages of drugs through the epidermis or its ducts, any effective influence is exerted on the tissues beneath. The epidermis likewise almost entirely resists the passage of morphine: hence opiate applications are far less frequently of benefit than is popularly supposed. On the other hand, atropine, although not a powerful depressant of the functions of the nerve-endings, passes readily through the epidermis; so too does aconitine, which has, however, in addition to its anæsthetic effects on the nerve-endings, an irritant effect on other tissues. Conium, like cocaine, has no action when applied to a surface covered with epidermis.

The exact part influenced by analgesics acting on the central nervous system is not known.

Substances which depress the higher cerebral functions, such as anæsthetics, chloral, bromide of potassium, are undoubtedly analgesics; but opium, which stands first and foremost of all drugs in the relief of pain, may act as an analgesic without exerting the slightest recognisable influence on the higher centres. We have no evidence that its influence is largely due to its local action on the nerve-endings; morphine applied locally will indeed relieve pain, but this may be due to its absorption into the blood. It certainly has no such depressing effects on the nerve-endings as cocaine; if injected subcutaneously the place of injection is a matter of indifference. Possibly it influences the grey matter in the cord along which painful sensations are conveyed, and the continuation of the grey matter into the brain; or it may affect the centre for the reception of pain.

The exact point, then, on which morphine exerts its effect in producing analgesia is still unknown. Such, too, is the case with the newer analgesics—antipyrin, antifebrin, and phenacetin. They likewise influence painful sensations in a manner for which neither their local action nor their influence on the cerebrum can account.

In choosing an analgesic the pharmacological influences of the drug, other than those which effect the relief of pain, are not to be forgotten; these secondary actions often limit their use.

Not only must we relieve pain where possible, but all forms of suffering also; and next to pain insomnia is perhaps the most distressing

of these forms. There is reason to believe the presence of certain elements and radicals in drugs gives them a power of depressing the tissues of the higher centres of the brain, and thus causing sleep. Almost all soporifics are derived from the fatty series, and many of them contain the elements chlorine and bromine. It seems probable that these elements, and also the fatty radicals, directly depress the functions of the nerve-cells in the cortex. The structure of hypnotics which do not belong to the fatty series, of which opium is the only one of importance, is not sufficiently known to enable us to ascertain to which of its constituent groups of molecules the effects are due. As in the case of analgesics, the use of soporifics is limited by the extent of their other pharmacological effects; chloral depresses the cardiac and respiratory centres, the former to a dangerous extent when administered in large doses. In the newer compound chloralamide this effect is in part avoided by the presence of a molecule of formamide, which contains a group NH_2 capable of stimulating the centres in the medulla.

Paraldehyde produces few special effects other than those procuring sleep, but its taste and the odour it gives to the breath are very objectionable; it is, moreover, much less certain in its effects than chloral. Sulphonal is also less certain than chloral; it is devoid of the unpleasantness of paraldehyde, but at times it disturbs muscular co-ordination, and in large and continued doses it may lead to the presence of hæmatoporphyrin in the urine, and death.

III. Principles of Administration

In the administration of drugs the chief point for consideration is the method by which they can best be brought, in the requisite quantity, in contact with the tissues to be influenced.

Methods.—Drugs may be introduced into the body in many ways, which may thus be shortly enumerated.

1. *By the Skin.*—The skin presents two pathways for the absorption of drugs, viz. through the epidermis or through the cutaneous glands. Whether drugs actually penetrate the epidermis is very doubtful, and it is found that the more effectual ways of securing absorption through the skin are those which appear most apt to carry the drug into the interior of the cutaneous glands, such as the inunction of a mercurial ointment, the exposure of the skin to the hot moist vapour of a calomel fumigation, or the solution of the drug in chloroform as a liniment. By this mode of administration we avoid any disturbing influence of the drug on the digestive organs, and young children can thus easily be put under treatment. The disadvantages consist in uncertainty as to the quantity of drug absorbed, and in the unpleasantness of greasy and sometimes dirty applications to a large surface of skin.

The following means are usually adopted for securing cutaneous absorption:—

Fumigations	Effectual.
Inunction of ointments or liniments . .	Effectual.
Endermic applications to surfaces denuded of epidermis	Effectual.
Electrical cataphoresis . .	Of doubtful value.
Plasters continually applied .	Of doubtful value.
Baths	Of doubtful value.
Medicated poultices and fomentations	Of doubtful value.

2. *By the Alimentary Canal.*

(*a*) By the stomach. The disadvantages of stomach administrations are—

(*α*) The drugs may be variously changed and decomposed by the digestive juice.

(*β*) They may disturb the digestive functions.

(*γ*) There is often delay in action, the rate of absorption being influenced by (1) the solubility of the drug; (2) the nature and amount of the gastric contents at the time of administration; and (3) the condition of the gastric mucous membrane; hence certain substances, such as sulphonal, are very uncertain in the time of their action.

(*b*) By the rectum in the form of enema and suppository. Absorption is slow from the rectum in the case of most drugs, and the dose needed is larger than when given by the stomach. Strychnine and tobacco are exceptions to this rule. Absorption may be greatly hastened by using drugs in more concentrated solutions and smaller bulk than is usual in enemas. Thus thirty or sixty minims of tincture of opium may be of little use when diluted with two or three ounces of water as an enema, but act quickly and satisfactorily when diluted with an equal bulk of water and injected into the empty rectum with a glycerin syringe.

3. *By the Respiratory Mucous Membrane.*—This is probably the most rapid means of entrance for drugs, owing to the large absorbent surface of the lung, and because the blood into which the drug has passed goes directly to the heart. Hence the extremely rapid action of amyl nitrite. This method of administration is limited, for the most part, in its application to drugs volatile at the temperature of the body, but injections into the trachea have been made; atomisation of fluids and insufflation of powders are commonly employed in local medication of the respiratory mucous membrane.

4. *By the Genital Mucous Membrane.*—Absorption through this channel is slow and uncertain. Usually the injections, pessaries, bougies, etc., used in this form of medication are employed for their local effect only.

5. *By Hypodermic Injection.*—This has the advantage of directly introducing the drug into the lymph-stream without any decomposition. The influence is rapid, and the dose of the drug can be accurately

graduated. The use is limited to drugs which are not irritating, and, usually, to those of which the dose is small, except in the case of saline solution or artificial serum.

6. *By Intravenous Injection.*—This is practically only used for the introduction of large quantities of saline fluid, though ammonia has thus been given.

7. *By Intraserous Injection.*—This has been employed in exceptional cases, but, so far as drug treatment is concerned, is of no value. The rapidity, however, with which absorption from serous cavities takes place is of importance in other relations.

Dosage.—The dose of a drug is not a fixed quantity, but must be determined according to the purpose for which the drug is given, and the conditions under which it is used. The conditions which chiefly influence dosage are age, sex, size and weight, and disease.

Age.—The usual rule is to take the adult dose as one year, and make a fraction, which has the age of the child for a numerator, and this age plus 12 for a denominator: this gives the fraction of the adult dose which is suitable for the child. Thus, for a child of six the dose would be $\frac{6}{12+6}$ or one-third of the adult doses. This is, of course, a mere approximation; moreover, each drug has to be considered separately in this respect. Children, for example, bear much larger relative doses of belladonna and arsenic than adults; but of opium, on the other hand, smaller doses. Should the decimal weights come into use Brunton's rule may be convenient. This is that the number of *grammes* in the full dose multiplied by the number of the child's next birthday and by four gives the dose in *centigrammes.*

Sex.—Women differ considerably from men in their reaction to medicine; the dose for a woman is usually considered to be four-fifths of that for a man.

Size and Weight seem to have less influence than would be generally supposed. It is only in exceptional cases—that is, where the size and weight are very small—that these factors need be taken into consideration.

The Present Disease.—This has often an important bearing on the dose. Any ailment which interferes with the functional activity of eliminating organs may seriously modify drug action. Hence, in kidney diseases, for example, opium has at times an exaggerated action.

As the dose of a drug has to be adapted to the changes in the tissues and organs it is meant to affect, and as the tissues of similar kind in different individuals are not influenced by the same amount of a drug, the dose which will effect its purpose has often to be arrived at by experiment — that is to say, by gradually raising it until a definite result is obtained.

Circumstances modifying the Influence of Drugs.—*Idiosyncrasy.*—One or more of the tissues may be unduly susceptible or insusceptible to the action of a drug. It is well known that the smallest quantity of calomel will salivate some persons, and a very minute dose of quinine

will cause a rash in others. The explanation of this is unknown, but even the simplest tissues vary in their reaction to drugs; the excised muscles of one frog, for example, may differ considerably in their ordinary reactions from those of a series of other frogs without any other ascertainable differences in the experiment. It is possible that the result may depend in part at least on food, for animals which have had potash added to their food for several days show considerable resistance to barium salts and veratrine.

Toleration.—When, on taking a drug continuously, the first effects decrease until they are no longer noticed, toleration is said to be established. In some cases this may be due to conditions causing increased elimination, or to the initiation of new chemical changes by which the drug becomes altered and even rendered inert. It may, however, also be due to some modification in the reacting tissue, caused by the continuous contact of the drug. It would appear as if toleration can be established more readily with some drugs than others; with opium, for example, it is easily established. For arsenic the toleration is not so readily established, unless indeed we accept the stories of the Styrian peasants. For chloral hydrate tolerance seems to become only partially established; patients can become habituated to larger doses, yet at times toleration seems temporarily to disappear, and a large habitual dose may at last have a fatal effect.

The duration of action of a drug is likewise dependent on the rapidity of its excretion and its adhesion to the tissues. The difference between drugs in this matter is enormous. Such substances as ammonia, ether, the nitrites, and alcohol produce their effects on the tissues quickly, and their effect as quickly passes away. An ordinary dose of ammonia or ether acts within a second or two; its effects do not last more than half an hour or an hour. Two grains of nitrite of sodium begin to act in two or three minutes, and its influence cannot be detected after three hours. Digitalis, on the other hand, does not show any signs of affecting the system for a long time, but its effect is long continued. It is manifest that this difference in the duration of the action of medicines should be considered in our combinations of them. It seems probable, for example, that if ammonia and digitalis are given in combination, the ammonia will have ceased to act before the digitalis begins.

Cumulative Action.—Some drugs are quickly excreted, others are stored up in the body, and may not exert their characteristic effect until a certain amount has accumulated. This is the case with digitalis, for example. When this drug is taken in small doses, its special effects are not seen, as a rule, for two or three days. Cumulative action of a drug is usually due in part to difficulty of excretion, but also to the stronger adhesion of its molecules to the tissues. Digitalis, as a matter of experiment, is washed out of tissues with much greater difficulty than many other substances. The reverse is the case with curare, which is so slowly absorbed from the stomach and so quickly removed from the tissues and excreted that, if the drug be taken by the mouth, a sufficient

quantity does not abide in them to produce its characteristic effect. Hence it must be given subcutaneously.

Sources of Fallacy in Therapeutics.—Some of the fallacies arising from defective observation and other causes have already been pointed out incidentally.

One is the assumption of pharmacological knowledge which does not exist. Some knowledge of the action of drugs on various parts of the body has been obtained, but concerning the effects of a large number definite information is wanting. Unfortunately, when knowledge is wanting, suppositions founded not on experiment but on fancy or on imperfect observation usually take their place. The reputed action of many drugs as cholagogues, diaphoretics, diuretics, etc., is founded on the most slender basis; yet it is constantly alleged as if it were founded on real knowledge. Of the alleged diaphoretic action of such substances as sassafras and serpentary, nothing certain is ascertained. Again, under what conditions the so-called "expectorants" produce their effects we do not know, and so forth; indeed, the action of most drugs on the tissues and organs is guessed at rather than known. Yet in therapeutic reasoning these hazy apprehensions are usually accepted as a basis for treatment.

A second source of fallacy is the persistence of old and baseless hypotheses. The opinions of Hippocrates and of Sydenham; those of Willis concerning the aiding of nature with regard to fermentation; of Boerhaave on obstruction of the vessels; of Brown on asthenia, still colour our therapeutic reasoning, and lingering like the nomenclature of their inventors, like it they influence thought.

Limits of the Utility of Drugs.—Drugs only act beneficially when they can exercise such influence on the morbid changes in tissues and organs as to restore the parts to a state compatible with systemic life. But in a large proportion of cases such restoration is impossible. Unfortunately for the reputation of drugs it is considered necessary to give them in all cases, even where it is manifest that the case is beyond the limits of drug treatment. The prevalent want of belief in drugs is largely due to the fact that they are expected to achieve the impossible.

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CLIMATE IN THE TREATMENT OF DISEASE

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THE Climate of a region or site is the combined effect of the atmosphere and of the nature of the surface in their relation to man. Of these the atmosphere, which is the product of many more or less varying agents, is the chief. The most important *qualities of the atmosphere* are:—

1. The chemical composition. 2. The organic and inorganic substances floating in it. 3. The temperature and its variations. 4. The degree of humidity. 5. The diathermancy. 6. The transparency and degree of intensity of light. 7. The density and pressure. 8. The electrical conditions. 9. The circulation of the air—the directions and the force of the winds.

The *climatic character of a locality* depends chiefly:—

1. On the distance from the equator. 2. The elevation above the sea. 3. The relation of its position to adjacent seas or large inland lakes, deserts, or marshes. 4. The predominating winds. 5. The nature of the soil: whether rock or dry porous ground, such as sand, allowing rapid percolation of moisture, and enclosing between the solid particles a large amount of air; or stiff, more or less impermeable ground, such as clay, peat, or marsh. 6. Configuration of surface: the amount of shelter, the position on a slope, terrace, or plateau, or in a valley; the aspect towards the sun, and possible amount of sunshine. 7. The mode of the cultivation of soil, whether arable fields or pastures, or heathland; whether the surface is bare, or covered with plantations of trees, or with more or less dense forests, consisting of deciduous or of evergreen trees or brushwood, or a combination of them; the density of population; the establishment of manufactures; the amount of drainage of the rural and the urban districts.

This article will be divided into three sections, as follows:—

First Section: Remarks on some of the principal elements of climate.

Second Section: Principal climatic regions and health resorts.

Third Section: Use of climate in the treatment and prevention of disease, with a sub-section on the use of "home" from a hygienic and therapeutic point of view.

First Section.—Remarks on some of the Principal Elements of Climate

1. *Composition of the Air.*—At one time it was generally maintained that the composition of the air was the same in all parts of the earth—at the tops of the mountains, on the sea, in rural and in town districts; but the researches of Tyndall, Frankland, R. Angus Smith, and others have shown that there are slight differences from the usually assumed composition, viz.—

Oxygen	20·96	
Nitrogen	79·00	
Carbonic acid	0·04	
in	100·00	volumes of air.

Although the differences in the proportion of oxygen rarely exceed $\frac{1}{10}$ volume, such a plus or minus is of great importance if we consider the large quantity of air which we inhale, and if we may assume that any deficit is generally associated with the presence or the increase of more or less injurious substances. R. Angus Smith found even in the same town considerable differences in the proportion of oxygen, *e.g.* in a northern suburb of London (Belsize Park) 21·01 per cent, in the middle of Hyde Park 21·005, in the Eastern district 20·86, in the tunnel of the Metropolitan Railway 20·70. In an open yard before a house more oxygen was found than within the rooms of the house. At the same spot he found differences under the influence of weather—more oxygen during and after rain than in dry and foggy weather.

Carbonic acid was first found by De Saussure as a regular constituent of the air in the proportion of 3·6 to 6 parts in 10,000; but its percentage varies considerably. Thus Angus Smith found in crowded law courts as much as 20, and in theatres even 32 in 10,000; and Pettenkofer found 20 to 58 in 10,000 in crowded schools at Munich. It is probable that air rich in carbonic acid is also rich in other impurities and in bacteria.

The air contains other gaseous substances, such as ozone, antozone, ammonia, which cannot be considered here, and the vapour of water, which will be discussed under humidity.

Very important are the solid substances floating in the air, the nature of which varies considerably at different localities and under different

conditions. They are partly inorganic, such as salty particles, silica, chalk, iron, and the like; partly organic, such as pollen, algæ, bacteria, fragments of hair, vegetable fibre, and insects. Some of these substances are innocuous, or nearly so; others are injurious. Ehrenberg, Schwann, and others directed attention to this matter long ago; but to Pasteur and Tyndall our debt is greatest. Pasteur showed the absence of organic impurity on glaciers, and its presence in large quantities in villages not far distant.

The recognition by Lister of the influence of these suspended matters on wounds, and the adoption of successful means to exclude them, mark an epoch in the history of Medicine; and their presence in the air of different localities deserves attention in the appreciation of climates. On this depends the septic or aseptic character of the atmosphere; and the predominant feature of the localities most beneficial in the treatment of pulmonary tuberculosis is the aseptic character of the atmosphere.

2. *Temperature* is a most powerful modifier of climates. We distinguish between radiant or sun heat, and shade or air heat. The rays of the sun heat the human body and other solid substances on which they fall very markedly, but only slightly warm the air through which they pass. The air would, in fact, allow the heat to pass through it entirely—it would be, to use a scientific term, quite diathermic—were it not for the watery vapour and occasionally other adventitious bodies, such as coal-dust, sand, and so forth, it contains. On the amount of these depends the degree of the diathermancy of the air, which is a very important factor of different climates. The more vapour and other added substances the air contains, the less powerful is the direct or radiant sun heat.

The shade temperature is due mainly to the warmth imparted to the air from the ground—water as well as land—previously warmed by the sun's rays. The shade temperature may, however, be greatly influenced by currents of air from distant regions, viz. warm or cold winds.

Melloni and Tyndall discovered that the water vapour is much less diathermic to the invisible waves of heat radiated back from the earth than to the direct luminous rays of the sun. This explains the protecting influence of the vapour on the ground, especially during the night; without it the greater part of the heat absorbed during the day would be rapidly radiated into space, and this indeed does occur when the air is very dry and the sky cloudless.

The nature of the surface of the ground exercises great influence on the amount of heat which is absorbed and reflected. We can only briefly allude to Frankland's instructive experiments on this subject. The nearer the colour of the ground approaches to white (snow, chalk cliffs, white walls, etc.) the more the direct sun heat is reflected by it, the less heat is absorbed; the darker the ground (grass, green leaves) the less heat is reflected, the more is absorbed. The ground which absorbs more heat from the direct rays of the sun can give out more heat during the night, and *vice versa*. The influence thus exercised on the

climate of a place is evident, and the white snow-fields of the Alps in winter form a well-known illustration.

We cannot enter on the distribution of temperature in the atmosphere on the surface of the earth, or on the great differences existing between the distances from the equator and the isothermal lines (with the same annual temperatures), and the isochimenal lines (with the same winter temperatures), and the isotheral lines (with the same summer temperatures). We must refer to Humboldt, Dove, Carpenter, Haughton, Scott, and others for accounts of the warming influences of the equatorial currents of the sea, and of the chilling action of the Arctic and Antarctic streams. This and other factors of climate are very clearly described by Dr. C. T. Williams in the Lumleian lectures on "Aero-therapeutics" (1894).

The temperature of the sea-coasts, however, is influenced not only by great sea currents; the nearness of oceans acts powerfully on the temperature of large tracts of continents—the range of temperature, as a rule, increasing from the coasts towards the interior. The Pacific, the Atlantic, and other oceans diminish the annual range of temperature on adjacent shores to 20° F. and less; while in the interior of large continents—as in the centre and north of Asia—the range may be 60°, 80°, and even 100° F.

Mountains and high elevations above the sea act likewise to some, though to a much less, degree as equalisers of temperature by lowering the annual range. In addition to this high mountain ranges act as shelters to the leeward regions; they condense the moisture on the side towards the sea, and render the air currents on the leeward side drier. We see this, for instance, by comparing the dry climates of Tibet and Cashmere with those of the windward side of the Himalayas, and those of the eastern side of the Rocky Mountains with those to the west of them.

Our knowledge of the influence of different degrees of temperature on the human body is still imperfect. Experiments have shown that cold acts as a stimulant and increases the amount of carbonic acid exhaled; but Pflüger has found a similar increase from heat, and Marcet came to the same conclusion from his observations on the island of Teneriffe: we must infer, then, that heat, up to a certain limit, also acts as a stimulant. Our general views on the influence of temperature are based partly on the effects of different seasons on the health of individuals; partly on the effects of moving during winter to warmer climates, and *vice versa*; partly on the consideration of the physical and mental constitution of races dwelling in different regions: but the co-existence of other climatic factors—such as moisture, light, rarefaction, or condensation of air—render inferences difficult, a difficulty further increased by variations in the manner of life.

It is necessary to distinguish between radiated or sun heat and shade heat. We do not yet know how great a degree of sun heat can be borne. It is certain that sunstroke is very rare in great sun heat in the pure and comparatively dry air of high elevations; and this seems also to be the case on the ocean. High shade temperature is, however, much less easily borne, and persons who can do hard work in a sun heat

of 120° become rapidly exhausted in a shade heat of 90°. Here, again, we must bear in mind that we cannot distinguish the effects of temperature from those of moisture, electrical condition, and movement of air. Different individuals bear heat very differently, and the manner of living influences the ability of bearing heat; many Europeans living in hot climates injure themselves by continuing to take the same kind and amount of food and stimulants as they do at home (Ranald Martin, Parkes, Fayrer, and others). However, as Parkes says, great heat in shade exerts "a depressing influence, lessening the great functions of digestion, respiration, sanguification, and, directly or indirectly, the formation and destruction of tissues." [1]

At climatic health resorts, however, we have not to deal with high, but with moderate degrees of heat, such as exist in summer in temperate and in winter in hot climates, namely, between 55° and 70° F. In such temperatures the organism loses less heat than at lower degrees. In strong persons, after long exposure to such temperatures, there is often a certain degree of lassitude, diminution of appetite, and impairment of the functions of digestion, respiration, circulation, and metabolism. Weak persons, on the other hand, often exhibit greater energy of all the functions of the mind and body, gain in weight, and are less liable to disease. Hence the value of such climates to permanently delicate persons, or to those temporarily weakened by disease, and to the elderly.

The effects of low temperature are likewise rarely observed alone; but it is certain that the body loses more heat and has to supply this loss. Increase of appetite, improvement of digestion, circulation, sanguification, and metabolism are in vigorous persons generally the results of moderate degrees of cold. The opposite is often the case with delicate persons, and especially so when cold is combined with damp and wind. It is particularly amongst old persons that the combination of cold with damp and high winds and absence of sun acts injuriously. The reports of the Registrar-General give ample proof of this. Thus in the last quarter of 1878, including two very cold months, the mortality of people above sixty was 24 per cent higher than during the same period in 1877, which was characterised by mild weather. The rate of increase amongst people below sixty was only 8 per cent. However, in combination with dryness of the air, light, sunshine, and absence of wind, moderate degrees of cold are beneficial even to many delicate persons.

The fact that cold is disagreeable to many persons induces them to regard it as injurious. That this, however, is not the case, is proved by the fact that the mortality decreases steadily from the tropics towards the pole. To quote from Michel Lévy's table in his *Hygiène*:—

From	0 to 20	degrees latitude,	1	death in	25	inhabitants.
"	20 " 40	"	1	"	35·5	"
"	40 " 60	"	1	"	43·2	"
"	60 " 80	"	1	"	55	"

[1] *Manual of Practical Hygiene*, 1878, p. 436.

It was formerly assumed that great equability of temperature is a necessary element of a climate useful in the treatment of chest complaints, and *vice versa*; but this again is not correct. There may be great differences between sun heat and shade temperature, and still greater differences between day and night temperatures—as in Alpine climates in winter—and yet such climates exercise the most beneficial effects, provided the invalid can obtain sufficient shelter.

3. *The humidity of the air* is almost as important a factor of climate as the temperature. Watery vapour is always contained in the air, but its amount is constantly changing by the ceaseless processes of evaporation and condensation. The degree of absolute humidity varies with the seasons, and at different hours of the day; it is generally greater with higher temperatures, and *vice versa.* The variations of relative humidity follow to some degree an opposite course: the relative humidity is, in general, lower in summer than in winter, and lower during the warmer parts of the day than during the colder; lowest, in fact, during the first hours of the afternoon and highest about sunrise. The variations are greater in summer than in winter, greater in inland than in marine climates; they are influenced by predominant winds, which when coming from moist regions render the air more humid, when coming from dry regions render it drier.

Saturation of the air leads to *mists* and *clouds*, and the periods and frequency of their occurrence are of great importance in the appreciation of climates. Mists are rarer at considerable elevations above the sea; clouds are more frequent at certain medium elevations, changing with the seasons.

The rainfall varies considerably in different regions, from 0 in the desert of Sahara and at some parts of the coast of Peru, to several hundred inches on the south-east slopes of the Himalayas, which are exposed to the moisture-laden monsoons. The amount of rain is not proportionate to the moisture of the air, for a region may be rainless, as Lima on the coast of Peru, in spite of a very humid atmosphere; and localities with considerable rainfall, like Genoa, may have tolerable dryness of soil and air. The number of rainy days does not correspond to the amount of rainfall. It may even be said, with some exceptions, that the number of rainy days increases with the distance from the equator, while the amount of rainfall decreases. The number of rainy days, the season when it rains oftenest, and the hours of the day on which the rain falls, are important matters to the invalid.

It is generally assumed that considerable rainfall is an injurious condition, but this is not always correct. Provided time enough be left for the invalid to take exercise and sit in the open air, rain is to some degree useful, as it has a purifying influence on the atmosphere. We must remember that Angus Smith found an increased amount of oxygen during and after rain, and cool and rainy summers in England mostly show smaller mortality than hot and dry ones. The notion that *snow* is injurious is even more incorrect. It is true that frequent melting of

snow is apt to produce catarrh; but if the snow remain on the ground without melting for periods of several months, it is to many invalids a source of benefit; for (*a*) it keeps the air free from the impurities rising from the soil, and from dust; (*b*) it increases the amount of radiant or sun heat by reflection; (*c*) it diminishes local currents of air by preventing the heating of the ground.

We have pointed out that the moisture of the atmosphere acts as a great regulator of the distribution of warmth on the surface of the globe, and that it is as essential to man as to vegetation; but it is difficult to define accurately the effects on man of different degrees of moisture, because the factor of moisture cannot be separated from other factors, especially temperature, light, atmospheric pressure, and wind. In dry air the evaporation from the skin and from the lungs is promoted, and this effect is increased if, at the same time, the sunshine be powerful, as in elevated regions. In moist air both are diminished. In moist and warm air the appetite and the vital energies become diminished, and there is often a tendency to diarrhœa and to affections of the abdominal organs. The growth of micro-organisms is favoured in such climates, and this probably is the reason why in some such, as at Lima, tuberculosis is frequent and runs a most rapid course. In moist and cold air the evaporation from the skin is checked, the surface loses much warmth, and rheumatic and catarrhal complaints are common. Climates with a moderate amount of moisture are more equable by day and night, and in sun and shade; the evaporation also is slight; while in dry climates, as we have already said, the opposite holds good. Climates with much moisture, especially when combined with low temperatures, often have a very dull sky, which may shut out the light and heat of the sun for many days and weeks; such climates are not exhilarating, but with proper hygienic management may allow perfect maintenance of health and vigour.

4. Our knowledge of the effects of slight changes in the *atmospheric pressure* is not well defined; the effects of the great diminution of pressure at high elevations will be discussed under Alpine climates.

5. *Light* is of primary importance. As is well known, light is necessary for the development of chlorophyll in plants; and it is a familiar experience that some persons after a few dull sunless days become depressed, disinclined to work, and dyspeptic, and that they regain their energy with the return of the sun. Home-sickness often develops in natives of foreign and more sunny countries after some sunless weeks in London, and disappears after a few weeks of sunny weather; but though we may suppose that absence of sunshine is the principal cause of such mental and bodily disturbance, it is difficult to say how much is due to concomitant circumstances, such as excessive moisture and to low temperature. W. F. Edwards showed long ago that light is necessary for the development of the perfect form of the Batrachia. Moleschott, Pflüger, von Platen, Tubini, and others have found increased absorption of oxygen and excretion of carbonic acid under the influence of light in

Batrachia and in some warm-blooded animals. H. Quincke's experiments prove that the oxidation of animal cells (of blood and pus) is increased under the influence of light. Many of the effects of light on the animal organism are, no doubt, due to its action on the centripetal nerves, and especially on those of the retina; but the researches of Quincke and of other observers show that light acts also directly on the cells and tissues without the influence of nerve centres.

The human body is influenced indirectly by the action of light on certain microbic parasites. Downes and Blunt, Arloing and Roux, had already shown that sunlight can kill bacteria, when Koch stated to the International Medical Congress at Berlin (1890) that it kills the tubercle bacillus within a very short time—varying from a few minutes to a few hours; and that even diffuse daylight does so, but requires from five to seven days. According to P. A. Komelevsky, solar light destroys the vitality of the Staphylococcus pyogenes aureus and albus, etc., in about six hours. He found that all portions of the spectrum, excepting the red and infra-red rays, powerfully affect the microbes. Professor Marshall Ward showed by experiments that the blue rays of the spectrum have the greatest power in destroying bacteria; while the red, orange, yellow, and ultra-violet rays do not affect them; our present experience seems to him, however, not conclusive with regard to all varieties of microbes. Dr. Arthur Ransome communicated to the Royal Society in 1890 experiments on the action of soil, air, and light on the tubercle bacillus; and again Drs. Ransome and Delépine infer "(1) that finely divided tuberculous matter—such as pure cultures of the bacillus, or 'tuberculous dust'—is rapidly deprived of virulence in daylight and in free currents of air; (2) that even in the dark, although the action is retarded, fresh air has still some disinfecting influence; and (3) that in the absence of air, or in confined air, the bacillus retains its power for long periods of time." These experiences seem of great importance in the explanation of the aseptic nature of the air in the high Alps, on the Riviera, in the desert, and elsewhere. It may further be mentioned that Buchner has shown that direct as well as diffused sunlight very rapidly kills bacteria suspended in water.

There is yet a third kind of influence of light on the human body, namely, on the skin. John of Gaddesden, a court physician in the reigns of the Edwards ("Rosa Anglica"), in treating a royal prince, a son of Edward I., for small-pox, prevented scars by having the bed-curtains and all surroundings made of red colour. The same treatment has been pursued by N. Finsen and Svensden, with the result of preventing the suppurative stage and the pitting. On the irritating influence of these rays interesting experiments have been made by Dr. Bowles, Unna, Hammer, Finsen, and others. Dr. Bowles, in his researches in the Alps on the effects of sunlight on the human body, was led to the conclusion that it is not heat, but those rays of shorter vibration at the violet end of the spectrum, which give rise to the phenomena of sunburn, and that rays reflected from snow are far more potent than rays direct from the

sun, or those reflected from rocks. He found that various colours applied to the skin prevented the harmful rays from reaching the delicate nerves and vessels beneath the epidermis, and quotes a singular case of an Indian officer who, having had repeated attacks of sunstroke, thinks that he has prevented the recurrence of the attacks by wearing an orange-coloured lining to his clothes.

6. *Of Winds*—a large subject—we can only speak briefly. They are necessary as purifiers of the air, though they may in special circumstances convey and spread disease. They often produce great and sudden changes in temperature, moisture, light, and atmospheric pressure ; and bring with them, so to speak, the climates of distant regions. Before selecting a health resort the winds prevailing at different seasons, at different parts of the day, and their character must be ascertained. Dr. W. Gordon has shown that in Devon, at all events, places exposed to the south and south-west winds have the highest mortality from pulmonary tuberculosis.

7. *Mountain chains* act as barriers to cold and to hot winds, and thus cause in the former case higher annual temperatures in the leeward localities, in the latter case lower. Their effects vary with their height, extension, abruptness, quality, and amount of vegetation; and with presence or absence of snow and glaciers. They exercise also a great influence on the quality of the atmosphere carried by the wind; they deprive, for instance, the moisture-laden, warm winds of a great part of their moisture, so that the climates to leeward of the chain are rendered drier and less equable.

8. Buchan (12 and 13) gives interesting facts on the effect of *drainage on the temperature of the soil.* The mean temperature of arable land is raised 0·80° F. by drainage ; cold penetrates undrained more quickly than drained land ; the temperature of drained land is more equable than that of undrained ; in summer the temperature of drained land is occasionally raised 1·8° to 3° F. above that of undrained land. These facts may throw some light on the discoveries of Bowditch and Buchanan with regard to the diminution of phthisis mortality by drainage.

9. The presence or absence of *vegetation* exercises a marked influence in all climates. Bare surfaces differ according to the conducting power of the ground. The covering of the surface by vegetation prevents more or less completely the direct fall of the sun's rays on the ground itself, and thus prevents it from being heated to the same degree as bare rock or dry sand ; and the plants themselves are never heated quite so much as bare ground on account of the constant process of evaporation. We have found the temperature above grass-land, and likewise clover, more than twenty degrees lower than above bare ground under great sun heat. The character of the vegetable covering, however, makes a considerable difference.

The influence of forests has been carefully studied by Buchan and Ebermayer. They found the temperature of the ground on which a forest stands to be several degrees lower than that of the neighbourhood. The difference is greater in summer than in winter, but the air

within the forest has a lower annual mean. In summer the cooling influence is specially marked during sunshine. The changes of temperature in forests are narrower and less sudden; the days are cooler, the nights warmer; the climate more equable. Trees acquire their maximum temperature in summer at about 9 P.M., while that of the air occurs between 2 and 3 P.M. "Hence trees may be regarded as reservoirs in which the heat of the day is closed up against the cold of the night." The relative humidity in forests is higher; in July about 10°, in January about 3·7°; forests lead also to increased rainfall; the air in forests being cooler and more saturated, the vapour of a moist wind on reaching a forest is condensed into mist and rain. There is less movement of air in forests, and they protect the adjacent land on the leeward side from winds and cold currents.

Second Section.—Principal Climatic Regions and Health Resorts

There are insurmountable difficulties in the classification of climates; the same degrees of latitude, for example, containing the most different climates. Many French writers, especially Lévy, Rochard, Fonssangrives, and Lacassagne, take the *mean annual temperature* with various modification; but the mean annual temperature is an imperfect guide in the treatment of disease, for localities with the same annual mean often differ very widely in range at the same season or at different seasons. Thus Torquay, Paris, and Odessa have approximate annual means, but the following table shows how different are their seasonal ranges:—

Annual Temperature.	Winter.	Spring.	Summer	Autumn.
Torquay about 52° Fahr.	44·0°	50·1°	61·3°	53·1°
Paris about 51·5° ..	38·4°	50·4°	64·5°	52·0°
Odessa about 50·4° ..	27·5°	45·8°	70·0°	50·7°

Thus the difference between summer and winter is for Torquay only 17°, for Paris 26°, for Odessa 42·5°.

A division according to the temperature of the seasons would be more useful, but places with the same winter temperatures may differ widely as to equability, sunshine, and humidity.

Several authors, English and foreign, adopt relative humidity as the main principle of classification (Vivenot, Walshe, Rohden, P. Niemeyer, Thomas), and this arrangement has its advantages; but other climatic factors may vary widely where the relative humidity is almost the same.

All such classifications appear to us so constrained that we should prefer to describe the several localities alphabetically, were it not that this would lead to much repetition and require more space.

We therefore propose to follow, with some modifications, the plan which has been adopted in previous treatises on this subject,[1] although we acknowledge its imperfections.

The sea exercises so powerful an influence on the climate of the localities adjacent to it that we will divide climates into A. *Marine*, and B. *Inland Climates.*

A. **Marine Climates.**—As fully marine climates can only be enjoyed on the ocean itself, we will begin with a short account of the ocean and of such sea-voyages as are best adapted to invalids, and then consider the climates of small islands and the sea-coasts.

I. *The Ocean and Sea-Voyages.*—The climate of the ocean is characterised by warmth, equability, and considerable atmospheric moisture. Its physiological effects are sedative to the nervous system, while at the same time appetite and digestion are much improved. The aseptic character of the air, moreover, acts beneficially both upon the air passages and the system at large. The advantages which it offers are almost absolute repose and facilities for an open-air life. Its drawbacks are the confined sleeping space, the discomforts of cabin life in bad weather, and in some cases the monotonous character of the food.

The voyages most suitable to the invalid are practically four:—(1) the steamship voyage to the Cape of Good Hope; (2) the sailing voyage to Australia; (3) the steamship voyage to Australia; (4) the steamship voyage to New Zealand round the Cape.

The voyage to the Cape occupies about twenty days, and is thus too short for much benefit in serious cases; but it has great value as a remedy for overwork or tardy convalescence. The heat in the tropics is rarely injurious, and there is no sudden transition to cold.

The voyage to Australia on a sailing ship gives the full benefit of the marine climate. Two or three clipper ships, with special accommodation for invalids, sail in September or October. The outward voyage takes ninety to a hundred days. The log of one of these ships shows the highest temperature to have been 85° F., the lowest 49° F., while the difference between one day and another never amounted to more than 7° F. (109). Except in a long calm in the equatorial belt the heat is not severely felt. To obtain the benefit of the change the patient should be moderate in his diet and take sufficient daily exercise. With such precautions selected cases will derive the greatest benefit from this class of voyage. The drawbacks to the voyage are the monotony of the life and the lack of fresh food. The return voyage might be made in a sailing ship round the Cape, or by steamer. A return by Cape Horn is generally unsuitable. The steamship voyage offers more frequent places of call, and a more frequent supply of fresh meat and vegetables. On the other hand, greater heat is experienced (in the Red Sea), and the greater speed of the vessel makes the changes of climate more sudden. The

[1] "Klimato-Therapie" in v. Ziemssen's *Handbuch der allgemeinen Therapie*, vol. ii. part 1. 1886. English translation by Dr. Port: Smith, Elder, and Co., 1885. And in "Climate and Health Resorts," in the *Book of Health*: Cassell and Co., London, 1883.

transition from the Red Sea to the Mediterranean is a considerable danger on the return journey. In modern ships the smoke from the engines is no longer a real drawback. The times of departure and return must be carefully chosen in order to avoid the hot months in the Red Sea and the monsoon in the Indian Ocean; it is wiser to return by San Francisco than to pass through the Red Sea in the hot months.

In the steamship voyage to New Zealand the weather encountered is very similar to that met with in the sailing voyage, but the time is shorter, and the food more varied.

We may add that in exceptional cases of hardy invalids summer voyages with whalers to the northern seas have been tried with fairly good results.

In the summer months yachting around the coasts of England, Sweden, Norway, the north of France, and in the Baltic, offers a good chance for enjoying the advantages of marine climates without much risk.

A combination of yachting with residence on land may occasionally be carried out with great advantage, especially in the Mediterranean during the colder months.

II. *Coast Climates, including small Islands.*—These climates, greatly though they differ amongst themselves, have some points in common: (1) The air is comparatively free from organic dust; (2) it contains a larger amount of moisture owing to the constant evaporation from the surface of the sea, and the amount of moisture does not vary much; (3) there is a constant renewal of the atmosphere by the air currents; (4) there is a greater equability of temperature, not only between different seasons, but also between the different parts of day and night, when compared with inland climates.

A striking instance of this equability of a climate almost entirely marine is given by A. Buchan (in his suggestive article on "Climate" in the *Encyclopædia Britannica*) in the island of Monach, situated about seven miles westward from the Hebrides, between 57° and 58° N., "in the full sweep of the westerly winds of the Atlantic which there prevail. The mean January temperature is 43·4°, being 1·8° higher than the mean of January at Ventnor, Isle of Wight (nearly seven degrees farther south), 0·8° higher than that of Jersey and Guernsey." On the other hand, the mean temperature of July is 55·0° at Monach and 62·4° at Ventnor. Monach has therefore warmer winters and cooler summers than an ordinary coast climate farther south.

The effects of the seaside, although varying considerably according to constitutions and localities, may be said to consist in improvement of the appetite, the mental and bodily energy, the condition of the skin, the sleep, and metabolism of tissues. Such changes are very useful in many cases of weakness without actual disease, during convalescence from disease and after surgical operations, in climacteric conditions, and in people "run down" from work, social exertions, or worry. These climates are invaluable in the physical training of children disposed

to scrofulous diseases and allied conditions. They require, however, a certain degree of resistance, and, in many persons, special attention to the action of the bowels. They are mostly unsuitable for chronic affections of the heart with great dilatation, for some kinds of asthma, and of skin diseases. One of the greatest advantages of seaside places is their usefulness in the prevention and treatment of scrofulosis, and through this also, in many cases, in the prevention of tuberculosis. To England belongs the merit of the recognition of this fact, which led to the foundation of the Royal Seaside Hospital at Margate, in 1791; but unfortunately this great step has not been followed up by the multiplication of such seaside hospitals; while on the Continent this kind of climatic treatment has been greatly developed. Many seaside hospitals have been established in France, Italy, Germany, and Austria; France, however, deserves special mention on account of the foundation of numerous well-arranged Seaside Sanatoria, mostly under the guidance of the "Assistance maritime des enfants scrofuleux." At Berck-sur-Mer alone this movement has led to the foundation of Sanatoria for several thousand scrofulous children of the poorer classes. Although the numerous varieties in the climatic conditions of different marine regions render subdivision necessary, yet different localities in the same region and very near to one another may present great varieties of climatic elements, such as aspect, elevation, degree of shelter, and so forth.

As the degree of humidity of the air exercises great influence on the equability of climates and on the functions of the body, we will, with Drs. C. T. Williams, Thomas, and others, adopt it as the principle of the greater subdivisions, and use the differences of temperature for the formation of sub-classes.

While adopting the subdivisions: 1. Humid marine climates; 2. Marine climates with moderate or slight humidity, we must confess that no rigid lines of demarcation can be drawn, and that some of the localities placed in sub. 1 might claim a place in sub. 2.

1. **Humid Marine Climates.**—There are great differences in this subdivision according to the temperature. We are, however, principally concerned with the *warmer* climates, of which *Madeira* may be taken as a type. The opinions on the climato-therapeutic value of Madeira have varied considerably. In former years it was considered by many authors as the best climate for consumption, while at present many regard it as the worst. We will endeavour to give a short description, and refer for further information to the works of Renton, Clark, Mittermaier, Lund, Grabham, Goldschmidt, Langerhans, and others. The Madeira Islands are situated between 32° and 34° N. and between 16° and 17° W. The climate of Funchal, the principal town, is remarkably equable; the mean moisture varies between 70° and 74°, but is subject to variations from air currents. The number of rainy days is mostly above fifty. The mean annual temperature is 65° F.—winter about 61°, spring 62°, summer 69·5°, autumn 67°. Lowest night temperature rarely below 43°; highest day rarely above 86°. Mean differences between night

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and day about 9°, from one day to another about 1·1°. Funchal is not exempt from winds, but the air is usually calm from 7 to 9 A.M., after which sea-breezes blow till 3 P.M.; land winds set in later at night. The air is free from dust and rich in ozone; the character of the climate is sedative, to some people relaxing. It has great power to allay coughs in chronic catarrh with irritability of the mucous membrane; but many people after some weeks feel depressed, lose appetite, and have a tendency to diarrhœa. A disadvantage of Funchal is the steepness of the hillside on which it lies, and the consequent difficulty of getting above the houses on foot.

As to the effect on pulmonary tuberculosis, the result of the experiment made by the authorities of the Brompton Hospital on twenty selected cases of consumption was not satisfactory, and we know ourselves of a rather large proportion of unfavourable cases; but, on the other hand, we have seen better effects than at most other places in elderly persons with much loss of lung and emphysema, in complications with albuminuria, and in weak and irritable people with rapid pulse (the erethic type). The beauty of the vegetation, the scenery, and the easy life of Madeira exercise on some persons so great a charm that it is impossible to dissuade them from going thither, even if they are told that they could do better elsewhere. More than once, especially in former years, patients would tell us they would rather die in the enjoyment of the subtropical beauty of Funchal than fight for life in the "ice-bound Alps," on the "dusty Riviera," or in "sunless England." And such mental conditions have a claim on our sympathy. This climate is more generally beneficial in cases of chronic bronchial and laryngeal catarrh, and in emphysema with scanty expectoration than in pulmonary tuberculosis; but in cases with copious discharges from the mucous membranes, atonic dyspepsia, and tendency to diarrhœa, Madeira and allied climates are to be avoided.

Similar remarks may be applied to the *Azores*, which are little used as climatic resorts.

The *Canaries*, with *Teneriffe* and the *Grand Canary*, have in common with Madeira the equability of the climate, but have a slightly higher temperature and are decidedly drier, so that they might claim a place in the subdivision of moderate humidity. They are mentioned here principally on account of their situation near Madeira. The heat of the day is tempered and the coolness of the night is diminished on Teneriffe by a layer of mist between 3000 and 5000 feet above the sea-level. On the Peak, above this layer of mist, Marcet found the climatic conditions very different, viz. hot days, cold nights, and great dryness of air. The Canaries have a greater claim as health resorts than Madeira, and offer good accommodation, but are much wanting in means of amusement (53, 35, 60). It must also be borne in mind that the best months in the Canaries are April, May, and June, a season at which other health resorts are apt either to be too hot or too cold.

Of *Mogador*, on the north-west coast of Africa, we owe a written

account, based on personal experience, to the late Dr. Leared, who described it as one of the most equable climates. Mean annual temperature 67° F., mean winter 61°, mean summer 72°, mean hottest month 80°, mean coolest 59°, relative humidity 78°. Number of rainy days 44, of clear days 270. It is under the influence of the Atlantic; is sheltered from the desert winds by the Atlas chain. Accommodation is as yet limited.

Cadiz, on the island of Leon, on the south-west coast of Spain, may be placed in this group. It partakes of the character of the Atlantic as well as of the Mediterranean, has about one hundred rainy days in the year, and an average relative humidity of 76°; the mean winter and spring temperatures are about 59° F.; the average daily range is only 10·5° F. We have seen some satisfactory results from this resort in early cases of consumption in weakly and irritable persons, but the hotels are situated in the midst of the town, and are scarcely suitable for invalids. Only persons, therefore, who have to earn their livelihood at the place ought to be sent there. *San Lucar*, in the same region, with a similar but somewhat drier climate, is recommended by Spanish physicians at the commencement of pulmonary tuberculosis.

In the *southern hemisphere*, where the sea predominates more than in the northern, there are several islands with moist and warm climates, which in especial circumstances may be used as health resorts, especially *Tahiti*, in the Society Islands, the *Tristan d'Acunha* group, the *Feejee* (Fidji, Fiji, or Viti), the *Friendly* or *Tonga Islands*; but the accommodation and hygienic conditions are as yet defective.

The groups of islands situated to the east of Central America, and comprised under the collective name of the *West Indies* (from 10° to 27° N.L.) find a place among the warm and humid marine climates. They possess rather uniform high temperatures, varying in the different islands between about 68° F. and 83° F. Their action is rather sedative and relaxing. Diseases of the digestive organs are prevalent; and only in exceptional cases can they be recommended to invalids suffering from irritable catarrhs of the respiratory mucous membranes. Dr. C. T. Williams (105) reports a favourable result in a consumptive young physician at Jamaica; R. H. Bakewell has a rather high opinion of Barbados; and we have ourselves seen some fairly satisfactory results in emphysema with chronic pulmonary catarrh, and in two cases of pulmonary tuberculosis—one at Jamaica, the other at Barbados; but unfavourable results have prevailed in our experience, especially through failure of the digestive system with loss of appetite and chronic diarrhœa, so that we can scarcely recommend these localities excepting in cases where the choice of climate is limited by other circumstances.

The island of *Cuba* is, as yet, not suitable as a health resort for the majority of invalids. The Isle of Pines, south of Cuba, had a good reputation amongst the Spaniards, who had established a military hospital at a small village called Nueva Gerona. A large number of cases of

pulmonary tuberculosis has been sent by Spanish physicians to this island, which has a sandy soil and is famous for its pines.

Bermuda has become a fashionable resort for North America in the late winter and early spring. It is too damp for tuberculosis, but more suitable for convalescents from acute illness and for those suffering from bronchitis and insomnia.

The climate of the peninsula of *Florida*, extending from 24° to 31° N., resembles that of the West Indies, but is less relaxing. In July, August, and September fevers are prevalent, but they are rare during the remainder of the year. Florida enjoys some reputation in North America as a mild winter resort for delicate persons suffering from emphysema, chronic bronchial catarrh, and early phthisis. The adjacent coasts of *Georgia* and *South Carolina* have somewhat similar climates, but they are more under the influence of the continent, and have lower average temperature and humidity.

Humid and cool marine climates are rarely used in climatic treatment, but they are very interesting on account of their great equability of temperature. The best-known localities belonging to Europe are the Hebrides, the Orkneys, the Shetland Islands, the Faroe Islands, and Iceland; and in the southern hemisphere the Auckland and Falkland Islands.

2. Marine Climates with Moderate or Slight Humidity.—Amongst the warmer localities of this sub-section those of the *Mediterranean coasts* are of the greatest interest to us. They are all under the powerful influence of this remarkable inland sea, which differs from the Atlantic and Pacific in its freedom from polar currents, and in its temperature, which down to its greatest depths (1500 to 2000 fathoms) is 54° to 56°; while in the Atlantic, outside the Straits of Gibraltar, the temperature at the same depth is only 35·6° to 37°. The Strait of Gibraltar is so shallow that it does not admit the polar stream of the Atlantic.

Although all the localities on the shores of the Mediterranean have some points in common, yet the several tracts offer considerable differences. The Riviera has the first claim on our attention.

The *Western Riviera* (Riviera di Ponente) stretches from Toulon to Genoa. The region consists for the most part of a plain from one to four miles in width, extending from the sea to the lower spurs of the mountains which everywhere guard the coast. From these lower slopes the mountains rise rather steeply to a height of from 2000 to 3000 feet, affording everywhere a shelter from the north, and generally from the north-east and north-west. The coast consists of a series of headlands, between which stretch gently curved bays, on whose shores the main resorts are situated. The characteristics of the climate are as follows:—

(*a*) *Warmth.*—Greater than that of other localities in the same latitude. This greater warmth is due to three causes: (1) The complete shelter from northerly winds; (2) radiation from the mountains during the colder parts of the day and year; (3) the presence of the Mediterranean Sea, which is some 5° warmer than the atmosphere. The

mean temperature for the six winter months varies from 50·8° to 51·5°; for the months of December, January, and February it varies from 47° to 49° F.

(*b*) *Dryness.*—Unlike most of the marine climates, the Riviera is distinguished for its dryness, the mean relative humidity being about 65° to 70° during the winter months.

(*c*) *Abundant Sunshine.*—During the six months of winter generally from 100 to 120 days are fine.

(*d*) *Small Rainfall.*—With few rainy days, the rainfall varies from 28 to 31 inches, and a great part of this occurs between the end of September and the beginning of November. In such a climate some hours of almost every day can be passed out of doors.

There are, however, several very distinct drawbacks to the climate: (*α*) The great frequency of high winds, principally in the spring, mainly from the north-east and north-west. (*β*) The great difference between sun and shade temperature, thus increasing the danger of chill. (*γ*) The rapid fall of temperature at sunset, which compels the invalid to return home before that hour.

The physiological effects of the climate are exerted for the most part on the nervous system; the climate is, with a good deal of truth, described as exciting. Sleeplessness is a common complaint on first reaching the coast, but in most cases soon passes off. Neuralgia, on the other hand, is often aggravated, and any hysterical or melancholic tendency is frequently made worse. Most persons, however, feel invigorated both in mind and body. Considerable care is necessary to avoid catching a chill. Exposure to sudden changes of temperature does not so frequently lead to a cold in the head, or tracheo-bronchitis, as at home, but more often causes an attack of diarrhœa or even of colitis.

The several resorts to be considered are:—

(i.) *Hyères*, situated about three miles from the sea. The mean winter temperature is 50·6° F. (Biden), and the relative humidity 78°. It is not, however, very well protected from the north, and is much exposed to the north-west, whence the mistral blows in the spring. In other respects, being somewhat more distant from the sea, it is not so exciting as are the other resorts; patients sleep better, and hysterical women rarely suffer any aggravation of their symptoms.

(ii.) *Costa Belle* or *Costebelle*, nearer the sea, is much better protected from winds, is more wooded, and not quite so dry.

(iii.) *St. Raphael* and *Valescure*, near Frejus. The former is near the sea-shore, the latter some short distance inland. They are not very well protected by mountains, but are surrounded by pine woods. The mean temperature is somewhat lower than that of the other resorts. They are better suited, perhaps, to a more vigorous class of case, and are not so exciting as the more easterly resorts. Some forms of asthma, neuralgia, and irritability of the skin do better there than at the more eastern places of the Riviera di Ponente.

(iv.) *Cannes* has a mean temperature of 50·85° for six winter months,

and a mean relative humidity of 73° (53); it is the largest of the mere health resort towns along the coast. To the north the protection is not by any means complete; the higher ridges of the Alps are too far removed from the sea to afford adequate shelter from this quarter. It is well protected, however, on the east and west. The mistral blows frequently in February and March. The majority of the patients find the climate bracing to the body and exhilarating to the mind, but it possesses to a marked degree the quality of an excitant to the nervous system. Invalids requiring much shelter can do better elsewhere than at Cannes; on the other hand, patients who require a bracing and yet warm climate will fare better at Cannes. Cannes enjoys the advantage of offering several residential localities with distinct varieties of climate. There is a warmer district near the sea, while more bracing and less exciting situations inland can be found on the Californie and in the district of Cannet. Patients who find the sea-shore too exciting often benefit by a removal to the latter.

(v.) *Grasse*, situated behind Cannes at an elevation of 1000 to 1100 feet, possesses a cooler climate, and forms a useful intermediate station during April and May for patients who find the heat in those months already too oppressive at Cannes. Many invalids sleep better, enjoy greater appetite and nerve energy at Grasse than at any other place on the Riviera, and many cases of asthma derive great advantage from residence at Grasse. Invalids affected with chronic rheumatism and rheumatoid arthritis are likewise more benefited at Grasse than at other localities on the Riviera.

(vi.) *Antibes*, situated on the headland of that name, now possesses an excellent hotel. It is perhaps not sufficiently sheltered for serious invalids, but hardier ones find it a pleasant climate and the centre of beautiful excursions.

(vii.) *Nice*, the largest town upon the coast, was formerly also its principal health resort. Latterly, however, it has somewhat fallen into disfavour on account of the piercing winds which visit it in winter and the irritating dust of the roads. The suburbs, however, of Carabacel, Cimiez, and Mont Boron present many attractions; they are moderately sheltered, and possess one advantage, namely, distance from the sea. Some persons when residing near the sea always suffer from constipation or other digestive disturbance, or are troubled by insomnia. Such symptoms are often entirely removed by a change to a residence a mile or two inland.

(viii.) *Villefranche* and *Beaulieu* lie between Nice and Monaco; both possess considerable advantages as to shelter and temperature.

(ix.) *Monte Carlo* is certainly one of the most sheltered situations on the coast. The presence of the gaming tables, however, offers an insuperable objection to its being seriously considered as a health resort.

(x.) *Mentone.*—Mean temperature for winter months 51·5°, mean relative humidity 72·8°.[1] This place, owing to the advocacy of the late

[1] Andrew, quoted by Marcet.

Henry Bennet, has perhaps obtained the greatest celebrity as a health resort. The town proper is situated on a tongue of land, which separates the bay into an eastern and western portion. The eastern bay of Mentone is admirably sheltered, the mountains rising on all sides sharply from the sea. It possesses the warmest temperature for the winter months of any resort on the Riviera. For cases requiring absolute shelter and warmth it is superior to any locality on the coast. Many persons, however, find it relaxing, while the steep rise of the mountains compels a residence close to the sea, with the ill effects which such a position exerts upon some constitutions. Another drawback is that there are at times disagreeable emanations from the old port. On the whole, however, in those qualities by virtue of which the Riviera climate is most to be esteemed it may be considered rich. The western bay, on the other hand, is less sheltered and more bracing, and, owing to the larger inland space, is adapted to a larger number of cases, though not so peculiarly suitable for a few. *Cap Martin*, in the vicinity, must also be mentioned. It possesses a great advantage in its large pine forest with beautiful sheltered walks.

(xi.) *Bordighera* is well protected from the north-east and the west, but through the valleys in the north-west the winds find access. The chief hotels and villas, however, are not situated by the sea-shore, and by the intervention of a spur of the mountains obtain adequate protection from that quarter. The temperature is for the winter months somewhat lower than at Mentone, but the climate is more bracing. The exciting effects of the Riviera climate are also not so marked as at places farther westward.

(xii.) *San Remo* has a mean temperature for six months of 50·55° (36); a mean relative humidity of 68°. It lies eight miles from Bordighera, and is well sheltered from the north and north-west, the mistral occurring but once or twice in the winter months. On the other hand the east wind is prevalent. The exciting effects of the climate are not so marked, but to some cases it will not be found so well adapted as the east bay of Mentone.

(xiii.) *Alassio*, twenty-eight miles east of San Remo, is well sheltered from the north and north-west and west; it is, however, exposed to the east and north-east. The lower spurs of the mountains are admirably sheltered from this quarter, and one or two hotels have recently been erected there.

(xiv.) *Pegli*, six miles from Genoa, the last of the resorts on the Western Riviera, is sheltered on the north, north-west, and west, but exposed to the east. It is, however, not sufficiently organised for the reception of other than the hardier class of invalids. The climate is more humid and less exciting than the westerly resorts.

By the end of October the weather will be cool enough to render any of these resorts suitable for invalids. It is rarely prudent to prolong the stay beyond the end of April, and a summer on the coast should always be avoided.

Eastern Riviera.—The continuation of the coast-line from Genoa to Pisa, usually called the *Riviera di Levante*, is less dry than that between Cannes and San Remo, and somewhat less protected from cold winds, the mountain chain being low and broken; otherwise there is some similarity between them. *Nervi*, near Genoa, has the principal claim as a health resort. It is fairly well protected from cold winds, and is less exciting than the majority of localities on the Western Riviera. The mountains come so near to the coast that the excursions for the invalid are limited; but those requiring repose find it helpful, the more so as there is not much temptation to social dissipation. *Rapallo* and *Santa Margherita* with *Porto-Fino* have latterly undergone considerable development. They are fairly sheltered, though rather more humid than the western resorts. *Sestri Levante* and *Spezia* are drier, but have less shelter. A rising health resort, for bathing in summer and shelter in winter, is *Viareggio*, about twelve miles north of Pisa. The shelter is principally due to the large pine forests in the neighbourhood.

Pisa, although six miles from the sea, may likewise be mentioned here, since the climate partakes both of marine and of inland characters. It is rather humid, and not well protected; the sky is often dull, but it is comparatively free from mists. The winter temperature is about 2° to 2½° lower than on the Western Riviera. It is less frequented now than in former years.

Genoa and Leghorn are too much exposed to be regarded as health resorts.

Southern Italy is rich in charms of nature and historical associations. The accommodation at the principal places is good, and the hygienic arrangements are improving; the climate is sunny, but by no means free from cold northerly and north-westerly winds, especially in spring. *Naples* has considerably gained of late by a good water-supply. *Castellamare*, *Sorrento*, and *Amalfi* have good autumn climates, and Amalfi is also well sheltered in spring. The islands of *Capri* and *Ischia* have many attractions, but are not sufficiently sheltered from cold winds, nor are they, as yet, thoroughly hygienic.

The *island of Sicily* is not much recommended by English physicians, nor can careful medical supervision be had there; but the great beauty of the country, and the many historical and archæological points of interest, have their favourable influence, and, combined with light and sun, have led to recovery or great improvement in many cases of overwork, of invalidism allied to the neurasthenic type, of rheumatism, slighter degrees of glycosuria, and tendency to premature senile decay in its various forms. The sirocco is occasionally irritating and depressing. Rain rarely falls in summer, but abundantly in late autumn and winter. The mean humidity is moderate—rather higher at *Palermo* and the north coast than on the east coast. Good accommodation, with fair sanitary arrangements, is to be found at *Palermo*, *Taormina*, *Acireale*, *Catania*, and *Syracuse*. The Hôtel des Temples at *Girgenti* is now open again.

On the south-west of the Mediterranean, *Tangiers* in Morocco is under

the combined influence of the Atlantic and the Mediterranean, and, owing to the former, approaches more the humid than the dry class of marine climates. The winter temperature is between 57° and 62°; the principal rains are in November and December. The late Dr. Leared and most of those who have resided there describe the winter and spring as delightful. The absence of carriage roads and the want of public security are for the present great drawbacks to its usefulness.

Gibraltar may be mentioned in this group, but it can scarcely be called a health resort.

Valencia has often been recommended on account of its mild and equable climate, but the effects of the irrigation of adjacent rice-fields are injurious to most invalids. *Barcelona* is rather sheltered by a range of hills from northerly winds, has good accommodation and fine walks. *Alicante*, like the whole coast of Murcia, is rather more dry. *Malaga* is described by Dr. Francis, who has studied the climates of Spain, as the mildest place in Europe; it has a dry soil, a south-easterly aspect, and is surrounded by a semicircle of mountains, but it is not sufficiently sheltered from the cold north-west winds. The temperature in winter is about 55° F., in spring 62°; the daily range scarcely 5°. The number of rainy days is about 40.

Algiers consists of the old Moorish town and the French settlement, of which the slope of *Mustapha Supérieur* and the road thence to *El Biar* are the most satisfactory localities for residence. The mean temperature during the invalid season, from the end of October to the end of April, is about 57° to 52° F., and the average number of rainy days is between 45 and 65. The soil is so porous that the rain seldom keeps an invalid at home the whole day. Rain usually falls heavily; there is rarely a drizzle. The sirocco is rare during the invalid season, but it blows occasionally, and exerts on some persons a relaxing effect, being hot, sultry, and dry. At few places is the difference of different winters so great as at Algiers; two seasons are rarely alike. As a rule, however, November, April, and part of May are like a fine summer in England; December to March like autumn, but with a greater share of sunshine. The air of Algiers is much less dry than on the Western Riviera; the hills are covered with evergreen shrubs and woods. The neighbourhood of Mustapha is rich in beautiful walks, and good carriage roads extend in every direction. People who stay the winter in Algiers may spend part of their time at *Hammam Meskouttin* or *Hamman R'Irha*, with their well-known hot springs; or at *Biskra*.

Biskra, a place of growing importance, is a union of several villages or urban quarters, lying among plantations of date-palms and evergreen trees, N. lat. 34° 51′, on the outskirts of the Algerian Sahara, at an elevation of about 360 feet above sea-level. It thus partakes of the characters of desert climates, excepting when northern winds prevail, and enjoys during the six colder months of the year many climatic advantages. It is much drier and sunnier than the neighbourhood of Algiers itself; but it is subject to violent winds which for days

together may prevent outdoor exercise. Another disadvantage is that the water contains too much salt for drinking and some cooking purposes. There is good hotel accommodation, and the place is likely to become a satisfactory health resort for fairly hardy individuals requiring warm and dry air. The railway journey occupies at present from Algiers two days, from Constantine one. There are hot springs a few miles from Biskra, at "Fontaine chaude," *Hammam Salahin* ("Bath of the Saints"), but the arrangements are not yet suited even for moderately fastidious people.

The Slopes of the Lebanon offer an excellent climate, only varying with the height above sea-level—the higher, of course, the colder. The view of the hills and of the sea below is glorious. In the summer months grapes, figs, and other fruits abound. The hotels are said to be good, especially at Alai, three hours' drive above Beyrout (or two hours by the new railway). The cost of board and lodging is usually about seven shillings a day per head. Dr. Canney, of Assouan, tells us that Brumana, on a fir-clad crest near Beyrout, is a pleasant health resort, and probably a little better than Alai.

Ajaccio in Corsica has a mean annual temperature of 62·5° F.—autumn 66·7°, winter 52°, spring 60·3°, summer 76·7°. The number of clear sunny days is great; the humidity is greater than on the Riviera. It is almost completely protected from cold winds. The accommodation is good. The climate is less exciting than that of the Riviera, and some invalids, who suffer from sleeplessness and neuralgia on the Riviera, feel better at Ajaccio. The best time is from the beginning of November to the middle of April. Summer stations can be found on the mountains for those who are not fastidious.

The *Sanguinaires*, small rocky islands near Ajaccio, have a still more decidedly marine climate, but the accommodation is as yet poor.

The climates of the shores and islands of the *Adriatic* Sea are very different from those on the western side of Italy. The predominant defects are the prevalence of the dry and cold wind from the north, the bora or tramontana—a land wind; and the moist and warm sirocco—a sea wind. The change between these two winds is accompanied by great variations in the temperature and in the relative humidity of the air, which are not well borne in irritable states of the nervous system or by pulmonary invalids.

Venice, the best-known of these localities, enjoyed in former years a great reputation in the treatment of consumption, and has the advantage of being free from dust and having good accommodation and artistic attractions. *Goerz*, near the north-west corner of the Adriatic, and *Volosca* and *Abbazia*, near the north-east shore, possess some shelter and beautiful positions, but cannot compete for English invalids with the Riviera di Ponente, although it must be acknowledged that Abbazia now has excellent hotels and many social attractions. Amongst the islands only *Lessina* and *Lissa* need be mentioned; they possess rather more equable climates than the shores, and some accommodation.

In the *Ionian Islands* the only place which has some pretension to be a health resort is *Corfu*. The beauty of the position of the town of Corfu is great, and the whole island is beautiful; but it is too much exposed to wind, and the temperature and humidity of the air vary considerably.

The *south-west coast of France* possesses a few localities which deserve to be mentioned.

Biarritz is fully exposed to the influence of the Atlantic; it is bright, and exercises on most people a bracing influence in spite of a rather high degree of humidity and frequent rains. It is not suitable to persons requiring shelter; but many old Indians with their complicated cachexias derive much benefit from this climate, which also offers a useful change to invalids wintering at Pau and Arcachon. *St. Jean de Luz*, a little to the south of Biarritz, has a similar climate.

A different kind of climate is that of *Arcachon*, which is situated on the shores of a large basin of salt water connected with the actual sea by a narrow channel. The influence of the sea is, therefore, considerably modified. The houses of Arcachon lie within a large pine forest, which is spread over the extensive dunes of the Atlantic. It is thus protected from the violence of the Atlantic winds, and the inland winds, too, are greatly mitigated by the trees. The climate is rather humid, equable, and unirritating, and the air in the "ville d'hiver" is impregnated with emanations from the pine-trees.

The western portion of *Southern California* presents several localities suitable for invalid residence. The country consists of a wide, fertile plain intersected by the lower spurs of the Sierra Madre and the coast range. The climate is warm and dry, with a large proportion of sunshine and small rainfall. The daily range is considerable, the prevalent westerly wind causing a fall of temperature in the afternoon. The damp, chilling sea-fogs, rolling in from the Pacific, are a drawback. On the other hand, the variety of elevation within a comparatively small compass fits it admirably for an all-the-year-round residence. According to Dr. Davidson a few hours' ride enables one to escape from the heat of summer to a cool and bracing atmosphere. Presenting some resemblance in climate to the Riviera, it shares some of its drawbacks, treachery amongst them. The chief resorts where good accommodation can be had are:—

Los Angeles, with a mean annual temperature of 61° and relative humidity of 69°; its suburb, *Pasadena*, at an elevation of 830 feet, and *Redlands*, higher up in the foot-hills, may also be mentioned. *San Diego* has a temperature of 54° in January and 69° in August; *Santa Barbara*, on the coast plain, a temperature of 50° to 55° in winter and 65° to 70° in summer. Monte Rey, the ancient Spanish capital, near San Francisco, is somewhat more exposed to fogs.

The coast climates of Great Britain and Ireland may be placed among the cooler marine climates with moderate humidity. Some localities might more justly find a place amongst the humid climates, but for the sake of brevity we will consider them together. Between the coasts of

these islands there are considerable differences, especially between the resorts on the east coast and those on the west; but certain features more or less common to all give them a special character. The mean temperature is much higher than is due to latitude. This is strikingly illustrated by A. Buchan. "If no more heat were received than is due to the position on the globe in respect to latitude, the mean winter temperature of Shetland would be only 3° and that of London 17°. But chiefly owing to the heat given out by the Gulf Stream during winter, and carried to the places by the winds, their winter temperatures are respectively 39° and 38°—Shetland being benefited 36° and London 21° from their proximity to the warm waters of the Atlantic." Part of this increase of temperature is due to the actual contact with the warmer sea.

Mild winters and cool summers, comparative absence of extremes, and a rather humid air, with many rainy days and comparatively many rainy hours, are the effects of these influences. The air, rich in water vapour, is less transcalent and translucent than in drier regions; hence direct sun heat and sunlight are less than on the Alps (Waters and Frankland) and on the Riviera (Marcet). On the other hand, the water vapour checks radiation at night and equalises the temperature of night and day. The chill at sunset is less than on the brighter and drier Riviera. The climatic characteristics are, therefore, comparatively high annual temperature, a fairly high degree of humidity, great equability as regards seasons and periods of the day, dulness of atmosphere with but a small amount of direct sunlight and sun heat, and more than average windiness. The combined effect produces health-giving and tonic, though not uniformly agreeable and exhilarating climates, which require some vigour of constitution to bear them. Speaking roughly, we may designate the west coast as warm and moist, the east as dry and cold; the western part of the south coast, as far as Sidmouth, as moist and specially warm; the line from Bournemouth to Hastings, including the Isle of Wight, as fairly dry and warm; the south-eastern part, with Folkestone and Dover, as approaching the characters of the east coast.

During the early part of the winter the temperature on the west and south-west coasts of England is between 2° and 6° higher than on the east coast; it gradually rises from the south-east to the south-west coasts. Towards summer this difference gradually disappears, and then sometimes the east coasts are warmer than the west.

We may roughly divide the seaside resorts into (*a*) *summer* and (*b*) *winter resorts*—adding, however, that some of the latter can occasionally be beneficially employed in summer, and *vice versa*.

(*a*) *Summer Resorts.*—There is no other country which is so well provided with good summer seaside places. The majority of them are situated on the east coast, and are decidedly bracing. Going from north to south we have Nairn, St. Andrews, Portobello, North Berwick, Redcar, Saltburn, Whitby, Scarborough, Filey, Bridlington, Hunstanton, Sherringham, Cromer, Mundesley, Yarmouth, Lowestoft, Southwold, Aldborough,

Felixstowe, Walton, Clacton-on-Sea, Westgate, Margate, Broadstairs, Ramsgate, St. Lawrence, Deal, Walmer, and St. Margaret's. On the south-east and south coasts, Dover, Folkestone, Sandgate, Hythe, Eastbourne, Seaford, Brighton, Worthing and Littlehampton, Bognor, Southsea. In the Isle of Wight, Sea View, Cowes, Ryde, Alum Bay, Freshwater, Bonchurch, Sandown, and Shanklin ; farther west, Swanage, Weymouth, Lyme Regis, Seaton, Exmouth ; the Channel Islands ; St. Ives, New Quay, Tintagel, and Bude ; Ilfracombe and Lynton on the north coasts of Cornwall and Devon ; Minehead, Weston-super-Mare, Clevedon, and Portishead on the Bristol Channel ; Tenby, Aberystwith, Barmouth, Beaumaris, Aber, Penmaenmawr, Llandudno, and Rhyl in Wales ; Southport, Blackpool, and Grange-over-Sands in Lancashire ; Douglas and Ramsey on the Isle of Man have almost thoroughly marine climates. Silloth in Cumberland, and Ardrossan, Oban, and Rothesay on Bute in Scotland have cool and rather humid summers, and the last has also mild autumns and winters.

The coasts of Ireland possess a mild, equable, and rather humid climate ; Bray, Howth, Kingstown, Dundrum, Holywood, Queenstown, and Glengariff are good representatives ; Bundoran and Kilkee are under the full influence of the Atlantic ; Portrush and Port Stewart in the north are somewhat more bracing ; Rostrevor and Warrenpoint are not quite exposed to the sea, and offer the advantages of beautiful inland country, protection from wind, and modified influence of the sea-air.

(*b*) *Winter Resorts.*—If we proceed from east to west we begin with Hastings and St. Leonards, which are less warm and somewhat more bracing than the localities farther west and south-west, and would be similar to the other places on the south-east coast were it not for the greater shelter which the downs afford from north-west, north, and north-east winds. Those requiring a warm, humid, and equable atmosphere are better farther west and south-west, but cases of atonic catarrh of the mucous membranes are mostly benefited in the autumn and winter, up to the end of February, when the east winds begin.

The Undercliff on the Isle of Wight, and the fair results obtained at the National Hospital for Consumption at Ventnor, are well known. This is also the case with Bournemouth and Boscombe, which offer abundant accommodation at the hotels and in numerous villas scattered about on the cliffs and in the pine woods ; these, unfortunately, are suffering from the rapid increase of the buildings. The wooded hills round Bournemouth and Boscombe are also suitable for summer and autumn residence to many delicate persons. They are generally described as too warm, but are in reality mostly somewhat cooler than the majority of inland residences, although they are, as a rule, warmer and less bracing than the localities on the east coast or the elevated inland places like Hindhead or Crowborough, or the more northern regions of Scotland.

Salcombe, Sidmouth, Budleigh-Salterton, Exmouth, Dawlish, and Teignmouth have all fairly warm and equable winters, and in their

climatic characters resemble Torquay, which, however, by its situation in a large bay surrounded by three hills, offers opportunities for extensive exercise on level as well as on rising ground, with ever-varying beautiful views. In spring the east wind sweeps round the protecting rocks and promontories, but is felt less severely than on the eastern part of the coast. Farther west, Falmouth in Cornwall claims our attention by similar qualities, and Penzance, which has less shelter from wind, but fair equability of temperature. On the coast of Wales, Pwllheli on the Cardigan Bay deserves our appreciation by its sheltered situation from north and east winds; and Llandudno, although principally a summer resort, also offers some advantages in winter. Grange on Morecambe Bay has good shelter. More northward the coast and the islands on the west of Scotland have a remarkably mild and equable, but at the same time humid winter climate; Rothesay, on the island of Bute, offers the best accommodation. Glengariff and Queenstown in Ireland, among the humid climates, have good claims to be regarded as winter resorts.

The climate of the north and still more of the north-west coast of France has, owing to the Gulf Stream, some analogy to that of the south and south-west coast of England, especially in summer. There is very little shelter in winter, but the climate in summer is rather more dry and stimulating than on the opposite coast of England. Dinard, Cabourg, Houlgate, Villers-sur-Mer, Trouville, Deauville, Étretat, Fécamp, Dieppe, St. Valéry en Caux, Tréport, and Boulogne offer satisfactory accommodation and good sands for bathing. The same may be said of Ostend, Blankenberghe, and Heyst in Belgium, and Scheveningen on the Dutch coast.

More bracing still are the seaside and island resorts on the north coast of Germany, exposed to the German Ocean; Borkum, Norderney, Baltrum, Langeroog, Spikeroog, Wangeroog, Wyk on Föhr, and Westerland on Sylt, but the accommodation at them is often primitive. The island of Heligoland has a much more decided marine climate.

The shores of the Baltic are less stimulating, but have beautiful forests. They are much frequented by Germans, and will be, sooner or later, much more appreciated by the inhabitants of the United Kingdom, especially the island of Ruegen.

B. **Inland Climates.**—We must be satisfied with the subdivision of the great variety of these climates into: I. Elevated or Mountain climates, and II. Lowland or Plain climates.

I. Elevated or Mountain Climates.—Great as is the difference between the various resorts belonging to this subdivision, elevation above the surrounding regions produces modifications in the climatic character which are common to them all. It is impossible by the mere elevation above the sea to define the limits which entitle a place to be called a mountain health resort. Latitude and the features of the surrounding country exercise great influence in this respect, which manifests itself quite as much in the nature of the vegetation as in the meteorological character; and from both combined we may draw some inferences as to

the probable physiological and therapeutic effects on the human constitution. In the low parts of Northern Europe, for instance, we find at an elevation of about 1200 to 1600 feet the vegetation peculiar to much higher elevations in Southern Europe, unless the nearness of the sea or the vicinity of higher mountains exercises modifying influences. In latitudes nearer the equator a much higher elevation is required to produce analogous effects. Thus J. M. Toner says, "On Chimboraza the palms, bananas, and oranges grow at 5000 feet; at 10,000 feet, Indian corn and wheat; and at 15,000, barley and the more hardy grasses." In a rough way we may assume that in Northern Europe (above 50° lat.) an elevation of 1000 to 1500 feet produces a mountain climate, unless nearness of the sea or of higher mountains interferes; while in the centre of Europe (between 48° and 50° lat.), 1400 to 2500 feet are required; between 47° and 48°, 2400 to 3500 feet; and in the tropics, 6000 to 9000 feet. The upper limits of elevation for health resorts likewise vary according to latitude and local circumstances.

We will begin our description with the *Swiss Alps.*

The general characteristics of the climate of the Swiss Alps in winter are:—

1. Low barometric pressure due to the altitude. 2. Great diathermancy of the atmosphere. 3. Low temperature. 4. Absence of fog and comparative freedom from clouds. 5. Low absolute and relative humidity. 6. Rareness of wind.

The patient is thus placed in an atmosphere of dry, still, cold, and rarefied air, and exposed to very powerful sunlight and sun heat.

What, then, are the effects of this climate upon the body? On arriving at one of the Alpine resorts the patient mostly first experiences a certain amount of difficulty in breathing; any exertion causes him to pant; frequently he cannot sleep; sometimes there is headache; the bowels are often constipated, and there is a general feeling of listlessness; thirst and dryness of the throat are prominent symptoms. On examination the respirations are found to be quicker and the pulse accelerated. Marcet (54) has shown that the amount of carbonic acid and water exhaled by the lungs is increased. Acclimatisation may take from three or four days to as many weeks; when this is established the pulse will have fallen to its normal condition, the respiration will be fuller and deeper than on the plain (94), the bowels regular, sleeplessness gone, and appetite improved.

These effects are merely those of altitude, as they may be observed in the summer to the same degree, and quite as frequently as in the winter. In the winter we have further to consider the bracing effect of the dry, cold air. The influence which the cold air produces is probably seen chiefly in increasing appetite and digestion; at the same time an increased amount of water is exhaled by the lungs, and the exhalation of carbonic acid is promoted by the cold air of the Alps (Marcet). Taken all together, it appears that altitude and cold combined produce a more rapid interchange in the tissues, and that in consequence of this

greater activity the tissues acquire an increased resistance to the action of micro-organisms. The paramount constitutional benefit of climate in phthisis must lie in the increase of this resistance of the tissues, and such is the unanimous opinion of all who have had much experience of the climates of high altitudes, and for these reasons :—

(*a*) Signs of constitutional improvement ; gain in weight and increase of appetite frequently precede any local improvement discernible by auscultation.

(*b*) Many patients, who have improved in the high altitudes, on going down to a lower level, where the atmosphere may be equally pure and dry, begin to lose weight ; while the disease shows signs of fresh activity.

This increased resistance seems to be brought about by the following factors :—

1. The large amount of time which is passed in the open air in a still atmosphere. 2. The tonic action of the dry, cold air. 3. The purity of the atmosphere. 4. The large amount of sunlight. 5. Perhaps a general tonic influence exerted by rarefied air upon the metabolism of the body.

In past years much more importance was attached to the extreme rarity of pulmonary tuberculosis among the natives of the high Alpine valleys. This rarity is probably to be explained by the outdoor life of the people and the smallness of the communities ; the absence or rarity of microbes is, however, well established.

The alleged fact that pulmonary tuberculosis is unknown amongst the inhabitants of the steppes indicates that altitude is not the only factor in conferring immunity ; an outdoor life is at least as habitual to these people also.

Increased resistance is brought about not only by increased appetite, but also by improved digestion and assimilation. The patient finds, to his surprise, that he can eat a heavy meal without any subsequent lassitude and torpor. Viault and Egger have shown that there is a somewhat rapid increase in red corpuscles in patients taken to a high altitude. Further, Bert's experiments in Peru (9) prove that the blood at high altitudes takes up a much greater percentage of its volume of oxygen.

Besides the constitutional effects of the dry, cold, thin air, there are certain purely physical effects produced upon the lungs themselves. Owing to the rarefied atmosphere each breath taken must, to supply the due measure of oxygen, be deeper than on the plain. The effect of this is to enlarge the circumference of the chest ; Dr. C. T. Williams (108) gives this enlargement at from one to three inches ; other observers are inclined to put it at somewhat less, though all are agreed that it does occur. A further result of this deeper manner of breathing is thoroughly to open up all the air vesicles, and thus to prevent any accumulation of secretions in them. After a more prolonged residence at high altitudes a state is reached which has been termed "hypertrophy of the lung." The chest

is enlarged to some extent and is hyper-resonant; the breath-sounds, instead of being weak, are puerile or exaggerated, but expiration is not prolonged. Whether this be merely a form of emphysema, or an actual increase in the respiratory area of the lungs, we cannot say; but after considerable experience, both of the natives of the high Alpine valleys and of consumptive patients, we can assert that this condition is very rarely associated with the ordinary symptoms of emphysema.

The principal resorts are :—

Davos (5200 feet). Is less windy than the other resorts, but receives less sun during the day. It is adapted to a greater variety of cases, and the accommodation and nursing arrangements are excellent. It is connected with Zürich and Chur by rail.

St. Moritz (6000 feet). Is more windy than Davos, but has a slight advantage in the matter of sun. It is admirably suited to more vigorous cases, but severe cases are better at Davos. The accommodation is good.

Leysin (4712 feet). Above Aigle. Is well protected and receives a large share of sunlight. A well-conducted sanatorium has been established there, and thorough supervision of the patients is carried out.

Wiesen (4771 feet). Chiefly used as a halting-place to and from Davos.

Arosa (6100 feet). Admirably sheltered, and at the Kulm receives a fair share of sunlight.

Les Avants, above Montreux (3500 feet), may be of use where the higher elevations are ill borne. An equally sheltered and sunny establishment at an elevation of over 5000 feet is being built.

The elevated resorts of the *Rocky Mountains* have, of late years, come into repute, and, thanks to the admirable accounts given by Dr. C. T. Williams (107), and the earlier ones by Denison and Solly, their main features are becoming well known. These resorts are situated in the State of Colorado, on the eastern slopes of the chain as it traverses that territory, at altitudes of from 5000 to 7000 feet. Meteorological observations tend to show that the climate is somewhat drier than that of the Swiss Alps, and has a very distinct advantage in the matter of sunshine; at Colorado Springs during the winter the sun shines during the greater part of the day for 165 days out of 182 (77), and the mean temperature is higher than in the Swiss Alps, the snow only lying for a few days at most during the winter. On the other hand, there is very much more wind and much more dust than in Alpine resorts. Electrical manifestations are a prominent feature of the climate, but as to whether these influence the body for good or ill, we know, scientifically speaking, nothing. The advantages of these resorts are :—

1. Altitude, the effects of which we have already discussed. 2. Dryness. 3. Abundant sunshine.

The climate, although not possessing some of the advantages of the Swiss Alps, is better adapted on the whole for an all-the-year-round residence; there is no snow-melting time, and the summer, although hotter, is more constant than in the Alps. Colorado, moreover, offers

better facilities for employment, sport, and exercise than any other resort. Subjects of constitutional erethism will probably fare even worse in Colorado than in the Swiss Alps. The accommodation is good, though, owing to the American fashion of meals, the food may not be so acceptable to the invalids as that of the Swiss hotels. It must be remembered also that the living expenses are heavier than in Europe.

The principal resorts are :—

Denver (5000 feet). A town of 150,000 inhabitants covering about five square miles. The mean annual temperature is 50°, the month of January showing a mean of 27·2°, and August 72·8°. Rainfall 14·17 inches (107). The accommodation is good, and the place presents all the advantages of a large town, though this can hardly be regarded as an unmixed benefit.

Colorado Springs (6022 feet). Seventy-five miles south of Denver; a town of 15,000 inhabitants. The mean temperature is 46·4°. Colorado Springs possesses an advantage over Denver in being almost exclusively a health resort, while the latter is a large commercial town.

Glenwood (5000 feet), on the Pacific slope, may also be mentioned; it possesses a most admirably conducted hotel. The climate is, however, damper than that of the other slope.

New Mexico seems to possess a valuable winter climate, but is practically unavailable, owing to the want of suitable accommodation, which, even at El Paso, is far from good.

The Andes.—Another class of mountain climates, which may with advantage be touched on here, contains those of the Andes, since it was by experience gained in them that Archibald Smith was first enabled to draw attention to the benefit in the treatment of phthisis likely to be obtained by residence in elevated regions. The main resorts are situated on the Pacific slope of the Andes—in Peru, and New Granada, at elevations varying from 8000 to 12,000 feet. The chief characteristics of these climates are :—1. Moderate warmth even in the highest resorts, owing to their proximity to the equator. 2. Remarkable equability of temperature. At Jauja, according to Archibald Smith, during a whole year the temperature never rose above 60°, or fell below 50°. 3. Considerable atmospheric dryness. 4. Abundant sunshine.

We have thus a temperate and extremely equable climate, with the additional advantage of rarefaction of the atmosphere. The admirable results obtained there among the consumptive natives of the plain prove the curative properties of the climate. Unfortunately, however, at none of the resorts is the accommodation good enough for invalids. For English patients, also, the length of the journey is prohibitive, except in the case of vigorous men with limited disease. For such as these, and for arrested cases, who wish to have a settled home in a good climate, and who are willing to build their own houses, these resorts offer decided advantages. Dr. Smith points out that patients, as a rule, do better at an elevation of 8000 to 10,000 feet than at the higher levels. The principal resorts are :—

Huancayo (10,000 feet), in Peru; the temperature of the whole year ranges between 51° and 63° (Williams).

Jauja, 10,000 feet, also in Peru, with a temperature ranging between 50° and 60° for the whole year round.

Quito, in Ecuador; a town of 80,000 inhabitants, situated at an altitude of 9500 feet, and with an all-the-year-round temperature of about 60°.

Santa Fé de Bogota, in New Granada, at an elevation of 8648 feet. The temperature is 59°, and is fairly constant all the season through.

In *India* there are several hill-stations, situated in the Himalayas and Nilgiris; but except for those who cannot leave India, they possess no particular advantages. The atmosphere is said to be very damp in the summer, owing to the heavy rainfall. The chief resorts are Simla (8000 feet) and Darjeeling (8000) in the Himalayas, with Ootacamund (7361) and Wellington (5840) in the Nilgiris. In considering the hill-stations of India we must bear in mind the nearness to the equator, by which the influences of altitude are considerably modified; and further, that the peninsula is surrounded, excepting at its broad base, by large masses of warm water. The periodical moisture-laden winds coming from these seas must, on reaching the colder mountain ranges, necessarily deposit a large portion of their humidity, rendering the soil damp, and the air emanating from it moist and impure.

Very different are the mountain climates on the north and north-west of the Himalayas, for the atmosphere on reaching them has lost a great part of its moisture on the southern slopes. Hence *Tibet* to the north, at 9000 to 11,000 feet, and *Cashmere* on the north-western chain, at 5000 to 6000 feet, possess healthy climates, and offer sites for most useful health resorts.

The *Eastern Alps*, with the Dolomites and the Tyrol, contain many beautiful localities which are gradually being provided with hotels suitable for delicate persons. In the *Dolomites* we may specially mention *Campiglio* (Madonna di San Campiglio), *San Martino di Castrozza*, *Schluderbach*, *Landro* or *Höhlenthal*, and *Cortina d' Ampezzo*. In the *Tyrol*, *St. Gertrud*, in the Sulden Valley, is above 6000 feet; *Trafoi*, 5000 feet; *Karer See*, 5010 feet; all the others are below 5000, and the majority below 4000, descending to about 2000: the *Mendelhof*, near Botzen; the hotels on the *Semmering Pass*; the *Brenner Pass*; *Gossensap*, near the Brenner Pass; *Innigen*, *Niederdorf*, *Toblach*, and *Neu Toblach*, in the Puster Valley; *Kreuth* and the *Achensee*; *Oberstdorf*; *Berchtesgaden*, with *Steinhaus* and *Vordereck*; *Zell am See*; *Garmisch*; *Partenkirchen* and *Kainzenbad*; *Aussee* and *Altaussee*; *Innsbruck*, with *Igls*.

There are, besides, many even less elevated localities, which, owing to the beauty of the situation and the comfort of the hotels, may be selected for shorter or longer stays, such as *Reichenhall*, *Salzburg*, *Ischl*, *Gmunden*.

Italian Mountain Stations.—The mountain ranges of *Italy*, excepting

the southern valleys of the Alps, included in the Alpine resorts (*Macugnaga*, *Gresoney*, *Alagna*), do not yet offer many localities which have adequate accommodation. *Ceresola Reale* in Piedmont, 5100 feet high, and *Abetone* and *Serrabassa* in the Apennines, at an elevation of about 5000 feet, *Courmayeur*, *Pré St. Didier*, *Monte Generoso*, and *Largo d' Intelvi*, near the Lake of Lugano, deserve to be mentioned ; and at lesser elevations, *St. Martin*, *Vesurbie*, *Ormea*, and *Certosa di Val Pesio*, in the Maritime Alps. *Perugia* and *Siena* are scarcely elevated enough to be regarded as hill stations, but they are delightful in spring and autumn.

In the *Pyrenees* there are various spas, which can also be used as climatic health resorts—*Barèges*, *Cauterets*, *Bagnères de Luchon*, *Bagnères de Bigorre*, *Eaux Bonnes*, but they are less bracing than the majority of the Alpine localities. In the south of France, Thorenc, near Grasse, must be mentioned as offering excellent accommodation at an elevation of about 3750 feet above sea-level.

In the mountains of the Auvergne *Mont Dore* has a claim to be regarded as a mountain health resort, but widely useful accommodation in this district might be provided on the *Puy-de-Dôme*, near Royat.

The health resorts of the *Black Forest* are of lesser elevation than those of Switzerland, but exercise, nevertheless, a moderately bracing though less stimulating influence. In addition to elevation, most of these localities have in their neighbourhood large pine forests, which exercise a purifying and equalising action. *Höchenschwand*, *Schönwald*, and *Rukstein* are the only places worth mentioning above 3000 feet; the other available localities are between 3000 and 1400—*Sand*, *Plaettig*, *Hundseck*, *Todtmoos*, *Schluchsee*, *Titissee*, *St. Blasien*, *Triberg*, *Freudenstadt*, *Allerheiligen*, *Rippoldsau*, *Griesbach*, *Badenweiler*.

Rather similar in character are some localities in the Vosges Mountains, of which *Hotel Altenberg* near Münster in Alsace, the *Hotel Schlucht* on the French frontier, *Gerardmer*, *Hohwald*, *Dreiaehren*, and *Odilienberg* are the best known.

Besides *Görbersdorf* and *Reiboldsgrün*, *Falkenstein*, and *Hohenhonnef*, well known as sanatoria for the treatment of consumption, the eastern mountain ranges of Germany are rich in well-wooded health resorts of local fame, ranging from 1500 to 2500 feet.

The *Harz* Mountains in the north of Germany offer many useful summer resorts between 1400 and nearly 3000, especially *Schierke* on the Brocken, *Clausthal*, *Andreasberg*, *Alexisbad*, *Harzburg*, *Ilsenburg*, and *Wernigerode*. The two first are already in use as sanatoria for phthisis all the year round.

The mountains and elevated places of *Great Britain* differ in climatic characters from those on the Continent. The atmosphere is more humid, less transparent and transcalent, the sun heat is less high, the temperature is more equable. There are scarcely any health resorts higher than 1000 feet, but the climate at such and at lower elevations is much more bracing than at similar elevations on the Continent. This is owing partly to the greater coolness of the summer, partly to the absence of

high mountains around them, preventing free access of air. There are no elevated winter resorts. The air on the Scotch and Yorkshire moors is thoroughly invigorating, but, unfortunately, the owners do not as yet tolerate hotels or sanatoria on them. There is, however, a considerable choice of localities, with good climates and fair accommodation. In Scotland—*Braemar*, *Ballater*, *Aviemore*, *Grantown*, *Forres*, *Strathpeffer*, *Blair Atholl*, *Pitlochry*, *Inversnaid*, the *Trossachs*, *Crieff*, and *Moffat*. In England —*Buxton*, *Harrogate*, *Ilkley*, *Gilsland*, *Malvern*, *Tunbridge Wells*, and *Frant*. In Wales, *Llanberis*, *Llandrindod*, and *Llangammarch* are best suited for those who want comfort combined with mountain air. It is much to be regretted that there are no good inns higher up on the mountains. In the south of England, Hindhead, Crowborough, and Tunbridge Wells have bracing air and good accommodation. On Dartmoor moderate accommodation is to be found at Princetown and Okehampton, but the air is much more humid than at the other localities just mentioned.

South Africa.—The district of South Africa which offers several localities possessing a climate suitable to invalids is the Karroo, a rolling desert-like country, varying in elevation from 2500 feet to 6000 feet. It is divided by the Nieuweld Mountains into two districts, Central and Upper Karroo. Of these the former slopes gradually southward, while the latter stretches northward as far as the Orange River. The climate is characterised by extreme dryness of the atmosphere, great heat in the summer, and small rainfall. The winter nights are cold, but, according to Dr. Saunders, the days are bright and sunny. The advantages of this climate are its altitude and the abundant opportunities it offers for outdoor life, without danger of taking cold; its drawbacks are the large amount of dust and the extreme heat of summer, though, owing to the dryness, the latter is not severely felt. The climate is bracing, but too exciting for persons of a nervous temperament. In timing the arrival of patients it must always be remembered that the seasons are the reverse of our own. The simple character of the accommodation, moreover, should deter the fastidious and any invalid not possessed of a fair amount of constitutional vigour.

Of the resorts whose capabilities have been so admirably summarised by Dr. Symes-Thompson (89), we may mention—

1. In the Great Karroo: Craddock (2855 feet) and Beaufort West (2792 feet).

2. In the Upper Karroo: Burgersdorp (4552 feet) and Tarkastad (4280), at which good results have been obtained in the treatment of pulmonary tuberculosis; also the flourishing townships of Aliwal North (4348), Kimberley (4012), and Bloemfontein (4500). Pretoria in the Transvaal is also rising into favour as a health resort. Ceres (1493), with its sanatorium, and Grahamstown (1800), form excellent intermediate stations between the coast and higher-altitude sanatoria.

Australia.—The regions of Australia possessing climates suitable to invalids are the inland plains, certain localities in the Blue Mountains, and the Australian Alps. The climate of the coast region, in which all

the chief towns are situated, is too variable, owing to the cold southerly winds and the hot winds which blow from the central desert. The mountains which fringe the coast from the South Australian border to Queensland have in the main a temperate, dry, and bracing climate. Although amongst the varieties of their climates there are probably some which would be of great value, yet the want of accommodation, except at two or three places, materially lessens their utility for the present, at all events. The available resorts are confined to those on *Mount Macedon* in Victoria, with *Catoomba* and *Mount Victoria* in New South Wales. The former, situated 44 miles from Melbourne, consists of Upper (3000 feet) and Lower Macedon (1660 feet), with the excellent sanatorium, *Braemar Wood End* (2500 feet). The mean annual temperature of *Macedon* is 53° F. The locality forms a good place of sojourn for those spending a short time in the colony (8).

Mount Victoria (3490 feet), 77 miles from Sydney, mean annual temperature 53° F., provides an excellent change from the climate of the inland plains.

Catoomba (3349 feet) is slightly more humid than the last-named.

The chief characteristics of the inland plains are extreme dryness of the atmosphere, abundant sunshine, and small rainfall. All these conditions mean ample opportunities for outdoor life. The drawbacks to the climate are the large amount of dust, the occasional occurrence of a hot north wind, and the possibility of a drought. The climate is undoubtedly bracing, the danger of chills is slight, and there are no marked ill effects upon the nervous system, such as sleeplessness.

The inland plains divide themselves into two districts: the Riverina in Victoria, lying to the north of the Murray River, and the Darling Downs in Queensland, an upland plateau (2000 feet) lying to the east of the former.

According to Dr. Lindsay, the heat in summer in the *Riverina* is considerable, though easily borne. In winter there are slight frosts, but the days are warm. The *Darling Downs* are somewhat cooler and less exposed to the hot wind. In both districts the accommodation is rough, and the climate is best enjoyed by residence on a station.

For some cases of phthisis the climate is admirably suited; the patient, however, must possess a good share of constitutional vigour, and must be ready and willing to content himself with the monotonous fare of a station or up-country township. Accommodation can be obtained at Deniliguin in the Riverina, and Warwick and Towoomba in the Darling Downs.

II. **The Lowland Climates.**—After having considered so many regions under the heads of Marine and of Mountain Climates, we can only glance rapidly at some of the less elevated regions not included in the former. Our attention is first claimed by Egypt.

Egypt owes its virtue as a climate chiefly to its being composed mainly of desert, so much so that the fertile spots included in the wastes

share, on the whole, the characteristics of the desert air. The main characteristics of the climate are :—

1. *Warmth*, the mean temperature at Cairo for the winter months being 58·3°. 2. *Wide Daily Range*, the difference between day and night temperatures varying from 35° to 19°. 3. *Low Relative Humidity*. 4. *Abundant Sunshine.*—Blue sky was chronicled on all but fifteen days during five months at Assouan, in the winter of 1892-93 (Longmore). 5. *Small Rainfall.*—Six rainy days only in five months were chronicled at Assouan in 1892-93. 6. *The extremely aseptic character of the air*, which is constantly refreshed by a breeze blowing over hundreds of miles of desert whence no emanations rise.

Most of the observations have been taken in localities situated on the cultivated land. Dr. Canney's observations, however (supported by the late Dr. Longmore's personal communications), taken in the desert at Luxor, and in other situations in Egypt, tend to show that the climate in the desert itself has a smaller daily range (17° in Luxor desert as against 32° in Luxor) and a lower relative humidity (54° in Luxor desert as against 69° in Luxor). The advantages of the climate are dry, warm, sunny days with cool nights, and a marvellously pure atmosphere. The drawbacks to the climate are the not infrequent presence of cold winds (though not to the same extent as on the Riviera), and the occasional occurrence of hot winds laden with dust; these are not only constitutionally most depressing, but intensely irritating to the lungs.

The physiological effects of the climate may be described as bracing to the organism as a whole, and sedative to the nervous system. Dr. Sandwith (70) gives records of 105 cases of phthisis; improvement took place in 72.

In Egypt the invalid can spend the greater part of the day in the open air, while at the same time sleep is encouraged rather than interfered with, and the nervous system is soothed. The danger of chill at sunset is, however, always present, and has to be guarded against as carefully as on the Riviera. The length of the journey and the great expenses of living necessarily exclude a certain number of invalids.

The chief individual resorts to be considered are :—

Cairo.—This should be avoided, as it is a crowded town, offering too many social temptations. Although the sanitation and water-supply of the hotels are good, the town itself is far from being in a hygienic condition.

Helouan.—About 15 miles from Cairo, standing in an oasis in the desert. There is more wind than at some other resorts; the accommodation is excellent. As it is a little above the level of the Delta, Helouan can be utilised also from November to January.

Mena House.—Near the pyramids, an admirably kept hotel. The climate in the late winter and early spring is much the same as that of Helouan. Owing to its proximity to the Delta the best season to visit Mena House is from the middle of February onwards; before that date

there is too much moisture in the air, owing to the drying up of the inundated plain.

The Nile Voyage.—This may be made in two ways: (*a*) by steamboat, (*b*) by dahabeyah. (*a*) The steamboat voyage is shorter, but less repose is obtained than on the dahabeyah. There is, moreover, far too much wind for serious invalids, and often a difference of 10° between different parts of the boat, and much more between sun and shade. Patients suffering from the throat often catch cold and become feverish. Here, too, the belief prevails that climate must do everything, and that the doctor need not be consulted. The long and hurried excursions to tombs and temples afford another source of danger to many invalids. Dr. Longmore, as the result of his experience, inclined to regard the voyage during the months of January and February as unsuitable to the pulmonary invalid, particularly so far as Lower Egypt is concerned.

(*b*) The dahabeyah, on the other hand, affords perfect leisure, while the contrasts of temperature are not so great. It is, however, costly, and the patient, unless he can afford a travelling physician, will be away from medical supervision; even in promising cases this is rarely advisable. During the months of January and February the dahabeyah should be kept south of Luxor (Longmore).

Luxor, situated on the Nile, 450 miles south of Cairo, possesses a milder climate than Lower Egypt, being warmer and not so subject to cold winds. Luxor is admirably suited as a residence for the invalid from the end of November to the middle of March. Moreover, the invalid can travel by train within a day's boat journey of Luxor; this is a great boon to those arriving late in the season, for whom the boat voyage is unsuitable. There is an admirable site for a sanatorium south of the hills above the tombs of the kings. Here, owing to the conformation of the country, the full advantage of desert air could be enjoyed to a greater degree than in any of the present resorts.

Assouan stands at the first cataract; it is somewhat more bracing, drier, and warmer, but, on the whole, a little more windy than Luxor. The accommodation is excellent, and admirable arrangements have been made for shelters.

On the whole the great advantages of desert air are not yet sufficiently available. We may say, however, that our experience of treatment by continued residence during several entire years in the Nubian Desert, under tents shifted from one place to another, has, in several advanced cases of consumption, given results which are altogether superior to any obtained from any health resort or from any other treatment. Yet if, at the site indicated near Luxor, a hotel were constructed on an improved plan as regards ventilation, verandahs, air-spaces for the night, food, and so forth, the conditions, to judge from the medical and scientific observations that have been made on the climate, would be nearly perfect under judicious medical guidance.

Pau, in the south-west of France, about 630 feet above sea-level, owes the peculiarities of its climate to its situation north of the Pyrenees,

not far removed from the Atlantic, and to its being surrounded by a wide circle of hills. Thus it enjoys considerable calmness of atmosphere, with the exception of occasional storms. The air is less dry, and the number of rainy days is greater than on the Riviera. The mean temperature from November to April is about 48·5° F., which is nearly 5° F. less than at the Western Riviera resorts, but it is rather more equable. There is less sunshine and sun heat; the difference between sun and shade and between day and night is less. On the whole the climate may be called sedative, and is therefore more suitable to cases with an irritable mucous membrane and an irritable nervous system than the Riviera (85).

Dax, in the south-west of France, has a somewhat similar climate, but is less sheltered and more under the influence of the Atlantic.

Arcachon, which has been mentioned under the marine climates, but has almost equal right to a place here, has some points in common with Pau.

The interior of Italy is rich in delightful localities, which may temporarily serve as residences to invalids, but few of them can be regarded as health resorts.

Rome will always claim the attention of physicians called upon to advise on climates, although it has long lost its great reputation in the cure of pulmonary tuberculosis. November is often rainy; December, January, and February are frequently cold; but March, April, and part of May are mostly pleasant, and may be useful in cases of arrested phthisis, cases with chronic bronchial catarrh, chronic rheumatism, gout, and mental depression, provided due care be taken to avoid over-fatigue in sight-seeing, and changes from the hot sun into cold galleries and churches. The climate of Rome should not be called relaxing; it may be said to take an intermediate place between Pau and the Riviera. The physicians residing in Rome describe the hygienic condition as much improved, especially in consequence of the excellent water-supply.

In the north of Italy the Lake district offers some climatic advantages, especially the *Lago Maggiore*, the lakes of *Como*, *Varese*, and *Lugano*, and the *Lago di Garda*. The climates of the different localities on these lakes are by no means the same, but all have in common the position to the south of the sheltering Alps, and the influence of the large sheets of water near which they are situated. They offer less warmth, less shelter, and less sun than the Riviera, and have more rain; but, compared with England, the number of clear days is greater and the relative humidity is smaller. The late Dr. Scharrenbroich, in a carefully written work on *Pallanza*, gives the relative humidity as 67·6°, the number of bright days during the colder seasons 185, of rainy 61. Pallanza, which is open throughout the year, has a mean winter temperature of only 39·1° F., which is scarcely more than the inland localities in the south of England, but in spring 54·4°, in summer 71·4°, in autumn 55·65°. The climate may be regarded as moderately dry and stimulating. That of *Locarno*, likewise open in winter, is somewhat similar, but is more

sheltered by the surrounding mountains. *Stresa* and *Baveno* are rather less sheltered, and are suitable only for spring, summer, and early autumn. On the Lake of Como, the *Villa d' Este*, *Menaggio*, *Cadenabbia*, and *Bellagio* are favourite resorts in spring and autumn. *Lugano* in winter and spring, according to Dr. Thomas, is slightly cooler than Pallanza. *Varese*, on the lake of the same name, deserves likewise to be mentioned ; it lies higher (1250 feet) than the localities on the four other lakes, which are between 600 and 1000 feet. The accommodation at *Orta*, with its beautiful little lake, is not yet quite so good as at the other places mentioned.

The *Lago di Garda*, south-east of the Lake district mentioned, at the foot of a precipitous mountain range, possesses a much more sheltered tract of shore than any of the other Italian lakes. It offers a very remarkable instance of the power of configuration, by which a limited Riviera-like climate is produced : here many delicate plants grow in the open air, and even lemon-trees on steep terraces. At a village, called *Gardone-Riviera*, a winter resort has sprung up which offers many advantages to those requiring much shelter, but unable to bear the immediate neighbourhood of the Mediterranean.

Arco, which has fair, though not the same amount of shelter, lies very near to the Lago di Garda, in an easterly direction ; it has for many years been used as a winter resort. All these localities are less dry, less warm, and less stimulating than the Italian Riviera, but less sedative than Pau.

We may here allude to two other localities, which have in former years enjoyed a wide reputation, especially in the treatment of pulmonary tuberculosis, viz. *Meran* with *Obermais*, and *Botzen* with *Gries*, both at the southern slopes of the Tyrolese Alps. They have bright sunny climates, with a certain amount of shelter and moderate relative humidity, but have no special claims as regards the treatment of tuberculosis.

Third Section.—Utilisation of Climates

We cannot regard climatic treatment in the narrow sense of treatment by the mere physical elements of climate, but we must include in it and avail ourselves of all the agencies associated or associable with the change of climate. Some of these agencies act principally on the bodily functions, while others bear directly on the mental functions, and through them on the organs and tissues.

Physicians who are consulted about the choice of a climate often meet with misconceptions on the part of the patients. The latter not rarely think that it is sufficient to know that they have "gout," or "dyspepsia," or "rheumatism," to enable the physician to recommend the "best climates" for those complaints : they do not consider that "gout" is often complicated with other affections, and differs so widely in different persons and constitutions, as to need widely different treat-

ment; and that the same is the case with "dyspepsia," "rheumatism," and almost all other chronic complaints. The patient, moreover, frequently regards the "climate of a place" as a fixed agent, comparable to a fixed dose of a particular drug,—say a grain of calomel, or three grains of quinine, or five of iodide of potassium,—while in reality the climate of a place during a certain season, say winter or spring, is an unstable agent, varying with the weather in the same year, and still more in different years. Some physicians are in the habit of saying that all climates are uncertain with the exception of Egypt, but after the personal experience of some winters in Egypt we cannot allow even this exception.

To answer a question frequently asked, *What is a good climate?* our answer is: A good climate is that in which all the organs and tissues of the body are kept evenly at work in alternation with rest. A climate with constant moderate variations in its principal factors is the best for the maintenance of health. It calls forth the energy of the different organs and functions, their power of adaptation and resistance, and keeps them in working condition. Such are the climates of England all the year round, and they belong to the most health-giving in the world. They produce the finest trees, the finest animals, the finest men, and are most conducive to longevity. They are, it is true, not the most agreeable or exhilarating climates; but the brightest and most exhilarating climates—such as those of Egypt, Spain, Italy, Greece, Asia Minor—are not the best for health and longevity; they are in many respects very inferior to those of England.

The best climates, however, for healthful development and for maintenance of health are not necessarily the best, may even be injurious to delicate or diseased persons whose organs and tissues have, temporarily or permanently, lost their energy, power of resistance, and adaptation. We must, therefore, endeavour to find *climates for invalids.* And here we must say at once there are no perfect climates for invalids. Relatively good climates for a given case are those in which the influences injurious to this case are either absent, or prevail only in a very slight degree: and where at the same time other influences exist which, when properly utilised, effect a general improvement of the whole constitution, and thus facilitate the recovery of the diseased or weakened organs and tissues as far as possible. Pure air and water, the possibility of spending a great part of the day in the open air, good hygienic and dietetic arrangements, and the presence of a good local physician conversant with the peculiarities of the climate and of the entire locality, are the most necessary conditions. The physician is, indeed, a very important part of a health resort and of a climatic cure, although the invalid is often disinclined to see this. Many lives are needlessly lost by trusting to the climate alone. The exhilarating influences of a climate, the many interesting objects of a place and its neighbourhood, and the social entertainments, are sources of temptation, lead often to undue exposure, to over-exertion, or to chills, and may destroy the chances of

recovery for ever; on the other hand, with the help of a judicious physician, not only may the dangers resulting from the defects of a place be escaped, but these very circumstances may also be employed to the benefit of the invalid. Too much importance, as already said, was formerly attributed to climate *per se*, too little to the management of the invalid by the local doctor. This is now generally acknowledged with regard to tuberculosis, but it is equally true with regard to other forms of illness.

The invalid must begin by studying, with the guidance of his physician, the following essential points :—

(1) The selection and arrangement of his rooms as to air and sun, and other hygienic influences. (2) The arrangement of his meals as to quality, quantity, and time. (3) How to be as much as possible in the open air. (4) What kind and amount of exercise to take, and at what times of the day, and when to rest. (5) How to clothe himself at different times of the day and of the season. (6) How to manage the skin. (7) How to occupy the mind.

Without due attention to these points many cases, even at the best resorts, are not benefited ; with it, good results can be obtained even at inferior localities.

In former times climatic treatment was almost limited to diseases of the respiratory organs, but at present we know that the treatment of almost every chronic deviation from health may be assisted by judicious change of climate. Our survey of the principal conditions in which climatic treatment is usually resorted to, must, however, be a summary one.

The Treatment of Pulmonary Tuberculosis by Climate.—Change of climate has been the hope of cure to the consumptive ever since the times of Pliny the elder. When we reflect on the widespread nature of the disease and the comparative failure of all ordinary means of treatment, we cannot be surprised that change of air should be invoked as an indefinable but potent agency which should at the last rescue the sufferer. This was the general conception running through all medical writings up to the eighteenth century. Coincidentally with the recognition of bronchitis as a distinct disease we begin to find the climatic cure of pulmonary tuberculosis proceeding on the lines which its apparently bronchial manifestations would warrant. In studying the rise and fall of health resorts in the past, it must be borne in mind that, during the eighteenth and first part of the nineteenth century, places with adequate accommodation were few ; and even these were subject to the political considerations of peace or war. Montpellier, the goal of the invalid in the eighteenth century, owed its position largely to the presence of fair accommodation and excellent doctors ; and yet, with all their querulousness, Laurence Sterne's criticisms read as singularly just. Lisbon, again, was one of the few places outside the British Isles not constantly threatened by the possibilities of siege or military occupation. Then came the vogue of Pisa, a civilised Tuscan town which, after the Great

Peace, was easy of access. After this, with improved methods of travel, the island of Madeira came into fashion. Later, partly owing to better communication and partly to the advocacy of a remarkable personality, Henry Bennet, the Riviera became the principal health resort. The next departure, namely the High Alps, changed entirely the point of view from which climatic treatment was regarded. Hitherto, from the earliest times, the general idea had been that the consumptive, like the sufferer from bronchitis, must be protected from every chance of catching cold. On these lines, his windows were closed, if he went out in wet weather he wore a respirator, and an out-of-door life in winter necessitated residence in some country where summer weather could be reasonably anticipated. In 1856 Archibald Smith called attention to the results obtained in the cure of pulmonary tuberculosis in the elevated cities of the Peruvian Andes. In the early 'sixties Spengler, a physician at Davos in the Grisons, commented on the extreme rarity of tuberculosis amongst the natives of high Alpine valleys, and suggested that a sojourn there might cure this disease. When this suggestion was acted on it soon became obvious, even to the most bigoted adherents of older methods, that the result far surpassed any that had hitherto been obtained. The experience thus gained modified the views as to what the essential principles of climatic treatment should be. It was obvious that consumptives could bear exposure to a considerable amount of cold without any increase of their catarrhal symptoms, or, in popular words, catching cold; and the idea that the climate which benefited bronchitic symptoms was the one indicated for pulmonary tuberculosis was necessarily abandoned. The growth of experimental pathology had meanwhile given rise to the doctrine of tissue-resistance, which at once supplied the key to the results of Alpine treatment. On analysing the factors which determined the success of Alpine treatment, it became clear that the most important of these was abundance of pure air. When it was found that patients could spend the greater part of their time in the open air under very diverse conditions, considerations of mere climate began to take a subsidiary place. On the other hand, it must be conceded that climate has a marked reinforcing effect on merely open-air life. A considerable amount of clinical experience is available on which to form an estimate as to what phases of the disease are most likely to be benefited by different climates. The cases likely to benefit by a stay in the Swiss Alps may be divided into two classes: (1) those who seek sanatorium treatment at the beginning of their malady, and (2) those improved but not cured at a sanatorium elsewhere in whom methods of regimen must be reinforced by climatic influences.

Dealing with the first class of case, patients who have become apyrexial, and in whom the extent of disease, whether unilateral or bilateral, is small, will probably still further increase their general resistance by a winter or more spent in the Alps. Some authorities state it as an axiom that the cure of pulmonary tuberculosis should be conducted in the climate in which the patient has subsequently to live. That is to say,

that, if he can be cured without the adventitious aid of climate, the greater the probability of the cure being permanent. With this premise, however, it is obvious that reinforcement by climate can exert no deleterious effect on the permanence of cure, which largely depends on surveillance and the incorporation of the hygienic measures of the sanatorium into daily life. Cases of pulmonary tuberculosis arising after a pleural effusion, in which pyrexia is moderate and the disease limited, should be sent to the Swiss Alps in preference to any other resort. The light of recent researches tends to the conclusion that practically all serous pleural effusions in the young are essentially due to definite tuberculous infection. So that, whether physical signs are present or not, the case should be treated as tuberculous.

The subject of constitutional erethism—persons, that is to say, with habitually quick pulse, light sleepers, and an irritable condition of the nervous system, had better not be sent, as their nervous system is seldom able to adapt itself to changed conditions; it therefore becomes over-stimulated, and a condition of irritable weakness results. There are, besides, a certain number of persons, elderly people especially, who cannot bear cold, in spite of the hot sun; for such persons Thorenc in summer would be better than most Alpine places. In this connexion Dr. Huggard, of Davos, has pointed out that persons with very rigid chest walls rarely do well at high altitudes. This rigidity is probably only one sign of a peculiar habit of body, injuriously affected by cold, and, as a clinical guide, is of great value. In cases of valvular disease or feeble heart-muscle acclimatisation is rarely likely to take place, and it would be wiser not to try the experiment. Cases of albuminuria are totally unsuitable. The selection of cases complicated by laryngeal tuberculosis must depend on the amount of irritability; in irritable cases the dry cold air, by inducing spasm, is apt to induce greater congestion. Where the extent of damaged lung is large, the case should on no account be sent, as the respiratory area will be unequal to the added strain.

In selecting cases for treatment in the Rocky Mountains many other factors must be taken into consideration. In the first place, it must be clearly understood that the opportunities for gaining a livelihood are limited. The professions and trades in the larger towns are overstocked, while farming without previous experience is disastrous. Conditions of life are so different that the emigrating consumptive Englishman stands but a poor chance against the native American. Further, the cost of living is at least three times as high as in England. Another drawback is the very limited amount of accommodation with adequate supervision for invalids. In fact, practically only rich and partially arrested cases should be sent to the Rockies. For such the climate is one of the most charming and health-giving in the world. Since the exciting effects of altitude are far more marked in Colorado than in Europe, highly strung individuals are entirely unsuitable.

Riviera and Alps.—The main virtues of the Riviera climate are that it permits the patient with proper appliances to pass the whole twenty-four

hours in the open air. The temperature is materially higher than during the English winter, the amount of sunshine much greater, fog is absent, and the atmosphere is much drier. The sea on the one hand and the vast expanse of barren mountains on the other render the atmosphere fairly free from impurities. The drawbacks of the climate are the occasional prevalence of cold and blustering winds, with the dust-storms which they raise, and the great difference between sun and shade temperature. The rapid fall of temperature at sunset, often amounting to 9° F. in as many minutes, which has been the bugbear of the invalid for forty years, has no really harmful effect on the tuberculous patient provided that he gradually accustoms himself to it, and there are no half measures about his open-air life. But the greatest drawback of all is the want of suitable accommodation. From being purely a health resort the Riviera has become the playground of a large section of the fashionable world. These people who have inherited or acquired wealth without entering into any of its territorial or political duties make the pursuit of pleasure their one aim in life, and rushing from one source of excitement to another is their normal condition. But with all this they are very nervous about infection, and consequently the hotels have closed their doors against the consumptive. Hence the difficulty of housing the consumptive. An admirable sanatorium at Gorbio, one or two minor ones elsewhere, and one or two nursing homes form the entire available accommodation. A villa with a properly constructed verandah for sleeping out at night forms an ideal residence, but is costly. No case should be sent to the Riviera without making very definite arrangement as to lodgings beforehand. The most suitable cases are, in the first place, those whose vitality is too low to enable them to stand the rigours of out-of-door life in an English winter; such cases often show marked improvement. Cases of true fibroid phthisis with marked retraction of the lung and displacement of the heart, and possibly with lardaceous disease of the kidneys, experience a marked relief from their most distressing symptoms, and live on for several years in comparative comfort.

Egypt is essentially suitable for those cases in which the bronchitic element is marked, or in which there is bronchiectasis. Wherever there is any form of tissue-degeneration, whether cardiac or renal, coupled with a fair amount of vigour, a winter in Egypt will yield the best results, but cases with diarrhœa should on no account be sent.

Australia.—With the improved methods of treatment at home now available, it can rarely be advisable to send a patient to Australia. Occasionally a patient with partially arrested disease who cannot stand the English winter may find employment there, but that is the sum of its utility.

South Africa, again, although endowed with a far better climate, has as yet so few facilities for the systematic treatment of pulmonary tuberculosis that, unless definite arrangements for board and so on can be made, it is better not to venture on the experiment.

The Ocean.—Since the introduction of systematic methods of treat-

ment, the open-air life at sea has fallen into disfavour. A doubtful case cannot get the necessary supervision, and may very probably lose more than climate can make up for. At the final stage of cure, when all disease is arrested, it may be of the greatest use. This aspect at the present day stands in danger of being overlooked. On the other hand, any one coming from the open-air life of a sanatorium would find the confined sleeping space of a cabin almost intolerable.

Sanatorium Treatment of Pulmonary Tuberculosis.—A certain class of resorts are of value not so much from their climatic conditions as from the advantages to be gained from the thorough and systematic use of fresh air.

All over Germany there is a large number of sanatoria for the working classes, financed and directed by the Government Insurance Boards. Besides these, *Görbersdorf*, in Silesia, the cradle of the method, is still continued; *Falkenstein*, in the Taunus, founded by a society of Frankfurt physicians, and until recently directed by Dettweiler, one of Brehmer's assistants, has been extensively added to; *Hohenhonnef*, in Rhenish Prussia, *Reiboldsgrün*, in the Saxonian Erzgebirge, and *Ruppertshain*, in the Taunus, are more recent. In the Black Forest there are *Nordrach*, the *Wehrawald* Sanatorium, and several others. In Switzerland there are Dr. Turban's sanatorium at *Davos*, and the *Schatzalp* above Aigle, Leysin, while almost every canton has a sanatorium for the poorer classes. In France, the sanatorium at *Gorbio*, above Mentone, and the beautiful "Mont des Oiseaux," near *Hyères*, may be mentioned. Italy as yet possesses no sanatorium, though one is in process of erection near *Sondrio*, in the Valtelline.

America has, until recently, been curiously behindhand in the establishment of sanatoria for the treatment of tuberculosis, though many exist for digestive and nervous disorders. An admirably managed sanatorium has, however, been conducted for many years at *Saranac*, in the Adirondacks, by Dr. Trudeau, to whom almost more than to any one else belongs the credit of establishing systematic treatment for tuberculosis in America. Dr. Loomis, of New York, has also for some years maintained a sanatorium. The State of Massachusetts, again, has established a thoroughly equipped sanatorium at *Rutland* in the Blue Hills. Both in Colorado and California adequate establishments are singularly lacking.

In the British Isles it is impossible to particularise the large numbers of private sanatoria which have sprung up all over the country, further than to say that the open-air principle of treatment is carried out to the full, and that for the most part the establishments are admirably equipped. Of public institutions more or less supported by charitable funds, several are situated amidst the heaths and pines of the Surrey Hills, such as the *Pinewood* Sanatorium, near Wokingham, *King Edward's Sanatorium*, near Midhurst, and the Brompton Hospital Sanatorium. Various counties have instituted sanatoria for the benefits of their own inhabitants—*Kelling*, near Holt, in Norfolk, for instance, is largely for

natives of Norfolk and Lincolnshire. In connexion with the subject of charitable institutions for the cure of pulmonary tuberculosis, attention should be drawn to the admirable manner in which the matter has been dealt with by the Charity Organisation Society, not only by liberal endowment of beds, but also in the infinite pains bestowed on the selection and subsidising of suitable cases.

Returning to the consideration of purely **climatic resorts**, *Madeira* is often more useful in consumptive cases with much irritability of constitution, and especially of the mucous membranes, accompanied by a dry cough; and in cases complicated with emphysema. It deserves a trial also in patients with laryngeal irritation. Patients with much expectoration, or with a weak intestinal mucous membrane, ought not to be sent to Madeira. The establishment of a large sanatorium under the guidance of Professor Paunwitz, of Berlin, is likely to increase the usefulness of Madeira.

The *Canaries* have a wider range of usefulness than Madeira; they are less humid, and the principal localities offer more chance for exercise on level or gently rising ground. Life there is, unfortunately, rather monotonous.

Pau and *Arcachon* are suitable in senile cases, and in complications with dry cough and constitutional irritability, where shelter from wind is important.

Ajaccio resembles the Riviera, but, owing to the larger amount of moisture in the air, is better for patients with dry cough and great irritability of the system. The same is the case with *Algiers*. On the other hand, cases with much expectoration and with albuminuria generally do better in Egypt and on the Riviera.

The treatment of pulmonary tuberculosis by climate in the *British Isles* may be regarded in two main divisions:—

1. *The provision* of a summer residence for those who winter abroad.
2. *The choice of a winter resort* for those whose condition or circumstances forbid their going farther afield.

The climate of England, although changeable, is, during the summer, bracing and sedative to the nervous system; in this respect it provides a most useful change to those who have wintered in the more exciting climates of the south. The choice will have to be made between the dry and bracing east coast, and the moister, more sedative, and warmer resorts of the south and west. For more vigorous patients, and particularly for those coming from the Riviera the east coast resorts—Hunstanton, Cromer, Yarmouth, Lowestoft, Felixstowe, Ramsgate, and Margate—are suitable during summer. These are often more beneficial to the Riviera patient than the Swiss resorts. The less vigorous, markedly catarrhal, and febrile cases will generally be more benefited by the resorts of the south and south-west—Bournemouth, Hastings, and Ventnor; or in the west—St. Ives, Ilfracombe, Torquay, and Falmouth. Amongst the inland places, Ilkley, Malvern, Tunbridge Wells, and Crowborough in England, Aviemore and Braemar in Scotland, may be

mentioned as excellent resorts for those who are injuriously affected by sea-air. Unfortunately, the English winter climate, owing to its changeableness and number of rainy days, precludes a great deal of that outdoor life so necessary to the well-being of the consumptive. Were the existing opportunities for outdoor life, however, more fully utilised—by sun-galleries, open-air shelters—at Eastbourne, Hastings, Brighton, far better results would be obtained, and the chances of good results have been vastly increased by the establishment of numerous sanatoria for rich and poor.

Dr. Williams' statistics (105) show a slightly smaller proportion of cures from winters at health resorts in England than on the Riviera, and distinctly less than those reported from the Swiss Alps. Although, therefore, the chances of cure are somewhat less than in the foreign resorts, yet the risks are smaller. Early cases, in which the course of the disease requires to be watched before deciding upon the trial of a foreign climate, may have the benefit of one of the home resorts. For cases of early consolidation, without fever, or for partially arrested cases, England is a safe abode all the year round. There remain, besides, as Dr. Wilson Fox (31) pointed out, a certain number of patients who, after trying foreign resorts without benefit, improve even in the most unlikely situations in England. Cases of laryngeal phthisis should seek the milder resorts on the south coast if there be any doubt as to the advisability of their going abroad. More severe and advanced cases will there find opportunities for a fair amount of outdoor life without the discomforts of an often fruitless journey abroad.

The choice of a locality rests between Bournemouth, Ventnor, Torquay, Penzance, Queenstown, and Hastings. Hastings is not adapted for other than the hardier cases; Torquay and Queenstown are rather relaxing, but well suited to patients with little constitutional vigour; Bournemouth and Ventnor are more suitable for earlier cases in the first and second stages.

In conclusion, it must be borne in mind that, though we have some few clinical rules which may help us in the selection of a climate, yet the issue of the selection lies mainly in the patient's own hands. Those patients do best who bear in mind that climatic change is the smallest factor in the treatment which is to restore them to health, and setting before themselves the recovery of health as their single aim, submit to a regulated manner of life, and to a sanatorium method of treatment.

Bronchitis, or **Chronic Bronchial Catarrh**, in young people is in general better influenced by mountain climate than by the sea-side; but in old persons the mountains are often injurious, and amongst the localities abroad the warm sea-side places of the Riviera or the climate of Egypt, of Algeria, of the south-west of France, or of the Canaries are beneficial; or Hastings, Bournemouth, Ventnor, Falmouth, Penzance in England. Whenever there is much expectoration the drier climates are better than the more humid; but if there be irritable cough without expectoration, the latter are preferable, such as Madeira, Algiers, Pau,

Arcachon, Torquay, Queenstown. In albuminuria, however slight, the mountain climates are to be avoided, while Egypt and the Riviera are often beneficial; the same is mostly the case with gouty bronchitis.

Emphysema with much expectoration is favourably influenced by dry and warm inland and coast climates; if it be attended with dry cough, the more humid climates of Madeira, Pau, Algiers, and Torquay are preferable. High elevations are not suitable, but moderate elevations are so in summer, especially those situated in or surrounded by pine forests.

Asthma often does not allow a decided opinion without a trial. Of two apparently similar cases one may bear a certain place well, the other not. In general, we can say that younger subjects are more benefited by long residence in the Alps than by any other climate or place. If possible their education should be conducted at high elevations. Senile patients with much expectoration ought to try Egypt or the Riviera; with little expectoration and irritating cough, Pau, Arcachon, Algiers, Ajaccio, or South Devon and Cornwall in England, or Queenstown in Ireland. Many asthmatic persons are better in London than elsewhere. In nervous asthma a cautious trial is required to find the most suitable localities.

Scrofula in its various forms requires improvement of nutrition, and mostly acceleration of tissue-change. Residence at the sea-side is most useful. Scrofulous children ought to be educated at the sea-side. The sea-coasts of England are pre-eminently adapted to this treatment; but in delicate children, with little reactive power, the winters ought to be spent at warmer coasts, such as the Mediterranean, or Ajaccio, or Algiers, or Biarritz, or Arcachon. Sea-voyages are likewise very useful. Alpine climates, too, offer advantages, but in the majority of cases the sea is to be preferred.

Gouty and **rheumatic affections** are aggravated by damp cold and winds. They require dry soil and warm and dry inland climates, such as the desert of Egypt or Algeria, and the southern slopes of mountains, or fairly warm sea-shores.

Affections of the heart include so many varieties that each class of case requires special management. On the whole, high elevation ought to be avoided, excepting in mitral cases with good compensation. Moderate elevations from 500 to 2500 feet with level walks are mostly preferable to the sea-shore. The winter should be spent in warm inland climates.

In **diseases of the kidneys** and **chronic catarrh of the bladder** warm and dry climates act beneficially, by rendering the skin more active, and thus relieving the work of the kidneys. Good milk ought to be obtainable at the resorts for these complaints. Elevated regions are mostly unsuitable.

The **diseases of the organs of digestion** are so multiform that it is impossible to lay down general rules. In convalescence from chronic catarrh of the colon and dysentery of malarious origin, dry elevated regions are useful. The same is the case with chronic flatulent dyspepsia, which often disappears rapidly on ascending, for instance, from Italy

to the Engadine. Dry and warm inland climates may likewise be recommended, especially where high elevations and sea-voyages are not suitable. Localities which offer inducement to open-air exercise deserve special attention. If, as frequently is the case, these complaints are only symptoms of nerve affections, the latter demand the principal consideration. Dietetic cures under strict medical supervision are in many cases necessary, and often ought to be carried out in well-arranged sanatoria.

Malarious affections in general are benefited by high elevations with dry and sunny air, and in summer especially by the air of glaciers.

Cases of **anæmia** and **chlorosis** require climates where the invalids can sit or lie the whole day in the open air without fatigue—such as sunny moderate elevations, and the cooler marine resorts in summer and the warmer in winter. Sea-voyages and yachting are useful for good sailors. Only a moderate amount of exercise is to be permitted, with easy mental and congenial social occupation, and inducement to take a proper amount of food.

In the treatment of **affections of the nervous system,** especially in those called *functional*, climate can take a fair share. In **mental depression,** and also in different forms of **hypochondriasis,** travelling, sea-voyages, frequent change of residence to places of historical, archæological, or artistic interest, which afford at the same time social attractions and facilities for open-air life and exercise, are often attended with excellent results. Rome, Florence, Naples, Sicily, Egypt, Athens and Greece, Palestine, and Asia Minor have in our experience often assisted recovery, and enabled the sufferer to return to home life and active mental occupation.

In that complex combination of nervous symptoms which is styled **neurasthenia**, change of climate can effect much good. It must be remembered that the sufferers from this malady owe their condition either to overstrain or to some essential nervous weakness which passes the breaking-point at even the moderate demands imposed by the ordinary conditions of everyday life; and according to the category into which the case falls, the general lines of treatment must differ. Many robust persons who have broken down will gain the greatest advantage by being placed at once under regimen and undergoing what is popularly known as a "rest cure." Where sleep has not been interfered with, and the general symptoms are those of failure of energy, a sojourn in the Engadine or elsewhere in the High Alps will work great good. A sea-voyage in others will effect wonders, but they must be free from any morbid fancies or general depression, and not sufferers from insomnia. The unhappily too frequent practice of sending moody or sleepless persons for a sea-voyage cannot be too strongly condemned. Only those who are familiar with life at sea can know the great temptations to suicide which are always present. Turning to the second class, that is, those with some inherent weakness in their nervous organisation, regulated systems of rest do far less good. Change of scene and interest will effect far more. The classic towns of

Italy and Sicily, or Egypt, will provide an intellectual interest; carefully regulated travel through them will yield far better results than any regimen.

Neuralgia must be treated according to its nature. If it be of gouty or rheumatic or dyspeptic origin, it falls under these several heads; if, as is often the case, it is one of the earlier symptoms of nervous exhaustion, the suggestions given above are applicable to it.

Diabetes, if acute, requires strict treatment at home; but in persons affected with chronic diabetes, or with different degrees of glycosuria (which are of widely varying nature), climatic treatment can be rendered more or less beneficial according to the nature of the case. In gouty constitutions, for instance, where corpulence is not rare, and where glucose in the urine often alternates with excess of uric acid, the indications are similar to those in gouty and corpulent persons. In invalids, where glycosuria is one of the manifestations of nerve failure, we may recommend, according to the degree of strength and resisting power, long residence at high elevations, or sunny inland and sea-shore localities. In addition to the considerations mentioned under the head of affections of the nervous system, we have in glycosuric cases to consider dietetics, and see that the plan of diet recommended can be carried out.

Polyuria is mostly a symptom, sometimes one of the earliest, of disorder of a nerve centre. As valerianate of zinc and similar remedies have a beneficial action on **diabetes insipidus**, so have Alpine climates combined with open-air life, but without fatigue.

In the state of convalescence from acute disease climatic treatment is often very useful, especially in **tardy convalescence.** We have to bear in mind that the whole system is weakened, and that there is increased liability to disease of different organs from over-fatigue in travelling, injudicious exercise or food, cold winds, damp, and so forth. It is, therefore, often advisable to begin with change to a good place within easy reach, and to proceed later to more distant localities. Great heat and cold are equally to be avoided, and much patience is often required. Important though this subject be from a climatic point of view, we must restrict ourselves to these cursory remarks, and leave more detailed suggestions to the writers on the several diseases.

Climacteric changes, in the wider sense of the term, frequently need climatic treatment. The deviations connected with the so-called "change of life" in women are well recognised; but in both sexes the quick rise to a higher stage of development, as well as the rapid descent to a lower stage, and also the delay of development, are often attended by a variety of disorders of the nervous system which manifest themselves in physical and mental disorders of the most varied nature. The development and the cessation of the sexual functions are the most perceptible signs of climacteric periods; but other important functions undergo like changes, and the harmony or equilibrium of the whole organism becomes sometimes disturbed for shorter or longer periods. The more invigorating climates are mostly preferable, but diversion of the mind greatly assists the adapta-

tion of the altered functions to the system at large. It must be borne in mind that there is increased "vulnerability," and that over-exertion and other risks must be avoided; otherwise the physical climatic elements of places need not be so carefully selected, while localities offering change, exhilaration, and mental recreation deserve special recommendation, such as Florence, Rome, the Gulf of Naples, Sicily, Greece, Spain, Asia Minor, Egypt, Algeria, the United States of America, the artistic centres of Italy, France, Germany, Holland, Belgium, and so forth, according to the nature of the individual cases.

Senile decay, whether simply natural or premature, is to be regarded as one of the climacteric changes; but in these cases we have to meet permanently diminished vital powers; hence the necessity of selecting localities which make more moderate demands on the weakened organism than at home, and at the same time gently stimulate the mental faculties. The first Lord Brougham showed his wisdom in spending the winters of his advanced life at Cannes.

We could go on enumerating almost indefinitely morbid conditions which can be benefited by judicious use of climatic changes, but for a short survey we have probably said enough. We must content ourselves with a mere allusion to the **prophylactic** value of climates. As we have alluded under the head of scrofula to the advisability of educating children with scrofulous tendencies at the sea-side, so we may say that in hereditary or acquired tendency to pulmonary tuberculosis education at well-selected elevated localities is much to be recommended—for instance, at St. Moritz, Davos, or "les Avants."

Moreover, we constantly meet with persons who have no definable disease, but are in a state of health, physical or mental, in which slight injurious influences may do mischief. In such states a judiciously arranged climatic change will often lead to the recovery of health and energy.

Utilisation of Home and Home Climates.—We will restrict ourselves in these remarks to the life of the invalid in English climates and in his own house. We must consider the disadvantages as well as the advantages. We cannot help acknowledging that there is some truth in the description which that sympathetic observer, the elder Dumas, puts into the mouth of D'Artagnan in *Vingt Ans Après*, the "pays où il fait froid toujours, où le beau temps est du brouillard, le brouillard de la pluie, la pluie du déluge; où le soleil resemble à la lune, et la lune à un fromage à la crême." Nor can we forget that we frequently meet with cases similar to that of a singer from Spain, whom we often found on her sick-bed humming words from Geibel's "Spanish Gipsy Boy in the North."[1]

Dieser Nebel drückt mich nieder
Der die Sonne mir entfernt
Und die alten lust'gen Lieder
Hab' ich alle fast verlernt.

[1] She was a consumptive patient who was unable or disinclined to eat, and could only be induced to do so by the constant promise to send her to Malaga, where she ultimately recovered.

Immer in die Melodien
Schleicht der Eine Klang sich ein;
In die Heimath möcht' ich ziehen,
In das Land voll Sonnenschein!

We must acknowledge that the climates of England are rather moist, that the air is often dull and sunless, that rain falls on comparatively many days, and is distributed over many hours, that the wind is often high and chilling, and that the shelter is limited. On the other hand, the hygienic conditions are better than anywhere else, the food is good, and the separation from the family is less complete. The climates of England belong, as we have said, to the most health-giving climates for the fairly vigorous, but are less good for the delicate invalid. If, however, a delicate person is obliged to stay at home or near home, it is often possible for him by judicious management to obtain great benefit by availing himself of all the advantages, and defending himself from the injurious influences of the home climates. It is doubly necessary for him to attend under medical guidance to the seven points which we formulated on page 328. If we carefully examine the good results obtained at foreign climatic health resorts, we often find that they are not so much due to the climatic advantages of those localities as to the hygienic and dietetic management and the whole manner of living. We see, for instance, that the results obtained at Görbersdorf, at Falkenstein, and at Hohenhonnef are as good as those gained at Davos, St. Moritz, and Colorado; and yet in the prominent climatic conditions—namely, the elevation, the number of sunny hours, the diathermancy of the atmosphere—the three former localities are decidedly inferior to the three latter; but in these the hygienic and dietetic arrangements, and especially the open-air treatment and the amount, the quantity, and the limits of exercise, are under careful supervision. We could give many instances from which we ought to gain hope that in our home climates, inferior as they are for the management of many delicate persons, satisfactory results may be obtained. A great source of difficulty is that at home the invalid is not inclined to devote the whole day to health matters, to walking or lying in the open air, to taking the necessary more or less numerous meals; but if it be once recognised that life depends on it, the majority of invalids will endeavour to obey. The sanatorium treatment should not be restricted to tuberculosis, but ought to be extended to other disorders, especially the treatment of affections of the nervous, digestive, and hæmopoietic systems.

Most important points for an invalid at home are the selection of a residence and the arrangement of the rooms he lives in. If it be possible for him to choose his house, let it be on a dry soil or rock, on a southern slope, and not at the bottom of a valley; let it be in the neighbourhood of woods, pine woods by preference, and let the woods be between the prevalent cold winds and the house. An abundant supply of good water is likewise necessary. The house ought to have a sunny verandah with

movable glass walls. All the rooms inhabited by the invalid should be towards the sun, and ventilated by day and by night. Couches for lying out of doors or in open verandahs or galleries, and seats with shelter, movable against the wind, or revolving shelters, ought to be provided. Such arrangements are expensive for single persons; but it ought not to be difficult to found, as already said, establishments under medical guidance for a number of cases, with diminution of expense and increase of convenience, with well-arranged walks, with large screens against the cold winds. There is, we know, a certain amount of prejudice in England against strict medical supervision, but if it were once realised that many lives can be saved in such establishments and under such judicious guidance, which, even at the best climatic health resorts, are otherwise lost, the opinion of the profession and the public would gradually become favourable to them.

It is a matter of great importance that the invalid who remains at his home or in his own country should feel that he is not doomed to die, that he should retain his energy and his firm will to regain his health. Every one of us has many pleasant memories of patients whose cases did not look promising at first, but who, by their firm will and their judicious and dutiful perseverance, entirely recovered in indifferent external circumstances. The qualities of energy, perseverance, and hope cannot be over-estimated in the treatment of chronic disease by climate.

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HYDROTHERAPY AND BALNEOTHERAPY

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Nomenclature.—Under the terms "Hydrotherapeutics" or "Hydrotherapy" the therapeutic use of water is considered, especially in its external application to the body. Practically speaking, the terms "Hydrotherapeutics," "Hydrotherapy," "Hydriatrics," and "Hydriatry" are synonymous, and we shall use them so. Some authors regard hydrotherapeutics as a subdivision of balneotherapeutics. It is, however, generally found convenient to regard the first part of the words balneotherapeutic and balneo-logy as derived from "balnea" in the late use of the word, *i.e.* in the sense of bathing resorts, or mineral water health resorts, that is to say, "spas."[1] Thus balneotherapeutics or balneotherapy comes

[1] In the seventeenth century when Spa in Belgium was visited from all parts of the world for the sake of its chalybeate springs, the word "spa" began to be used by the English to signify any medicinal spring or mineral water health resort.

to signify everything relating to "spa-treatment," and in the article on balneotherapy we shall deal with the internal and external uses of natural mineral waters. "Thermotherapy," or treatment by heat and cold, is intimately connected both with hydrotherapeutics and balneotherapeutics. The therapeutic resources of many spas include natural thermal springs used for hot baths, natural vapour baths, and various kinds of mud, peat, and sand used for hot applications. All these have, therefore, to some extent to be considered under Balneotherapy. Yet under hydrotherapy it is customary to discuss not only hot baths and douches, but also vapour baths, and all kinds of hot-air baths, including electric light baths. Medical baths and artificial mineral water baths are also sometimes considered under hydrotherapeutics, but the internal use of artificial mineral waters belongs to balneotherapeutics, or to ordinary pharmacotherapeutics. The word "hydropathy" (cf. "homœopathy," "allopathy"), which is perpetuated in the so-called "hydropathic establishments" ("Hydros") of Great Britain, belongs really to a time when the "water-cure" was more empirical and more in the hands of unqualified practitioners than at the present day. The word should certainly be avoided in medical works, since the termination "pathy" ("arthropathy," "myopathy") is at present used in quite another sense.

A. Hydrotherapy

History.—Hydrotherapy was known to the ancient Greeks and Romans, and regular bathing of the body and keeping of the skin in a healthy condition were, like the athletic training of the body, held by them in high esteem. It is possible that a reaction from the excessive luxury of later Rome, when the thermæ became "pleasure resorts" ("Balnea,[1] vina, Venus corrumpunt corpora nostra"), helped to bring baths into the neglect into which they fell amongst the early ascetic Christians.

In Italy and France hydrotherapy made a start in the fifteenth and early in the sixteenth century, and was even applied in mental diseases, as narrated in one of Poggio's tales. At the end of the seventeenth century Sir John Floyer wrote on hydrotherapeutics in England, and in the early eighteenth century F. Hoffmann wrote on the subject in Germany. About the middle of the eighteenth century J. G. and J. S. Hahn treated febrile diseases with cold sponging, and one of them, when attacked with typhoid fever, had himself treated by this method, modifications of which have been so widely adopted in modern times. In the latter part of the eighteenth and early part of the nineteenth centuries, in spite of the results by W. Wright and James Currie in England, and in Germany by Reuss, Frohlich, Brandis, and Horn, hydrotherapeutical treatment was again falling into disuse, when, soon after 1820, Vincent Priessnitz, originally a small farmer of Graefenberg in Silesia, began to

[1] Doubtless baths and douches were used to stimulate the enervated body and make further dissipation possible.

treat every kind of ailment, chronic as well as acute, by hydrotherapeutic means. He added to the external applications the abundant internal use of water, and with this treatment he combined active exercise and a very simple diet, prohibiting tea, coffee, and all alcoholic beverages. Priessnitz at different periods made considerable alterations in his hydrotherapeutic measures. Originally he packed patients for several hours in dry woollen blankets, covered with feather beds, before applying cold affusions; later he substituted packing in wet linen sheets for several hours, followed by a full bath or a douche; still later he frequently employed a cold wet pack of fifteen or twenty minutes' duration, repeated several times in the same day. He introduced the method of rubbing the whole body with a cold wet sheet instead of the full bath; and made extensive use of partial baths for the hips, the hands, the arms, or the feet, of wet abdominal belts, and of wet applications on different parts of the body. The success of his measures, combined as they were with a simple diet and exercise in a healthy mountainous country, was in many cases considerable; but the indiscriminate, too energetic, and protracted use of his methods often led to unfavourable results. The system was beginning to be regarded as a sort of quackery, when, about the year 1850, establishments were placed under the superintendence of regularly educated physicians, who studied the physiological effects of the different methods, and modified them according to the requirements of individual cases: they also added pharmaceutical remedies when required. To the works of the more modern authors, Winternitz, Hayem, Strasser, Buxbaum, Baruch, Matthes, and Schweinburg, the reader is referred for details of the subject not given in the present article.

Although England has taken such a prominent position in the use of baths in health, especially the daily morning "tub," it is remarkable that, as compared with French and German hospitals, the London hospitals are still very badly furnished with douches and other means of hydrotherapeutic treatment.

Modes of Application.—Amongst these are the ordinary full bath at different temperatures, hip-baths, shower or rain baths, wrapping in wet towels, affusions, douches of various kinds, and many forms of local applications. The temperature may be varied during the application (alternating douche, Scotch douche). Among the many forms of medicated baths only a few can be mentioned here. Brine-baths, to imitate sea-baths, can be made by adding about 10 lb. of sea-salt to thirty gallons of water. Alkaline baths of thirty gallons contain about six ounces of carbonate of sodium or three ounces of carbonate of potassium. Acid baths can be made by adding about twelve ounces of diluted nitro-hydrochloric acid to thirty gallons of water. The common bran and mustard baths need not be described. Aromatic and pine baths are made by adding a decoction of aromatic plants, such as lavender or fresh pine leaflets, or an extract or essence of pine leaflets to warm water. Mercurial baths have been used in the treatment of syphilis. Baths can also be made to imitate those of natural mineral waters. Natural tepid

effervescent salt baths, as used at Nauheim in the treatment of chronic cardiac disorders, may to some extent be imitated by dissolving 2 or 3 per cent common salt and 2 or 3 per mille calcium chloride in plain water, which is then charged with carbonic acid from a cylinder of the compressed gas.

The varieties of hydrotherapeutic application are very numerous, but most ends which can be attained in the present state of our knowledge can be arrived at by the judicious use of a very small number of appliances.

The internal use of plain water as a therapeutic agent, much employed in the old "water-cure," is now generally but an adjuvant to other methods of treatment.

Vapour and hot-air baths (and the local vapour douches occasionally made use of) may, as already mentioned, conveniently be classed with hydrotherapeutic appliances. In the Turkish and Russian baths the patient is placed in a chamber heated with watery vapour; but a vapour bath may also be taken in a box not including the head, and both hot-air and vapour baths are often given to renal patients in bed. In the Roman bath the hottest chamber, the "Calidarium" or "Sudatorium," is heated by dry air to a temperature of 130° to 140° F. (sometimes higher), and perspiration is generally more copious than in the cooler vapour baths (in vapour baths a heat of more than 122° F. is not borne comfortably), though some persons apparently commence to sweat more readily and with greater feeling of comfort in moist air than in dry air. These baths may be followed by soaping, rubbing, douching, and a plunge into cold water. In electric light baths ("radiant heat baths") and in local dry air (Tallermann apparatus) baths of much higher temperatures can be employed than in the ordinary Turkish, Russian, and Roman baths. Electric light is now much employed for local and general (whole body) hot-air baths. The patient sits in a kind of box or lies on a couch with the head excluded; the temperature at which the whole body radiant heat baths are given is 200° to 350° F., or even higher, and it is maintained that owing to the action of the light as well as of heat, in some individuals at all events, sweating is produced without accelerating the heart's action to the same extent as in the ordinary vapour and hot-air baths. In some individuals free sweating is not readily or comfortably produced by any kind of bath.

Treatment by hydrotherapeutic means depends chiefly on the reaction of the organism to cold and heat, and, but for old custom, most of the subject might be discussed equally well under "thermotherapeutics" or "thermotherapy" as a heading. A mechanical stimulation is added to the purely hydrotherapeutic effect by the impetus of the water in douches, and to some extent by the bubbles of carbon dioxide in the waters of Schwalbach, Nauheim, and elsewhere; the addition of a little mustard has a chemically stimulating effect, and a bran bath diminishes the irritability of the skin; stimulation of the skin may also be increased by friction and massage. Care must, however, be taken that stimulation does not exceed the powers of the organism, and supervision by a medical

man is necessary for the proper regulation of the treatment in every case. Each case must be considered on its merits, and hydrotherapeutic treatment may be associated, according to requirements, with change in diet, air, and the surroundings of the patient; or with a course of mineral waters or internal medication.

Action and Physiological Effects.—What has been called the "hydrotherapeutic reaction" is the natural reaction of the organism to cold or heat; the organism thus endeavours to defend itself against the action of these agents. The skin of the body, unprotected by any natural covering, reacts more readily to cold and heat in man than in animals; in most races this sensitiveness is increased by the habitual use of clothes: thus the clothes form a sort of zone around the body, in which the temperature stands, with tolerable regularity (according to Winternitz), at about 90° F. In order, therefore, to obtain the "hydrotherapeutic reaction," it is necessary that the water should have a temperature some degrees above or below 90° F. It is obvious, also, that on account of its greater specific heat and greater coefficient of heat-conductivity, water is much more active than air of the same temperature in inducing the reaction. On the proper bringing about of this reaction the result of hydrotherapeutic treatment largely depends.

Cold-Water Treatment.—When a healthy man jumps into a cold bath, or has a cold douche applied over the whole or a considerable area of his body, he receives an impression of cold, shivers, and, after an almost involuntary pause in breathing, takes a very deep inspiration. The skin is pale, and, owing to the contraction of the unstriped muscle-fibres, presents the appearance called "goose skin." When the man gets out of the bath, or sometimes even whilst he still remains in it, these first effects give place to the phenomena of the "reaction." The skin then becomes slightly reddened, and an agreeable subjective sensation of warmth is experienced. He breathes more easily, and has a general feeling of comfort and capability for exertion. This is the "hydrotherapeutic reaction" to cold; it depends in degree and rapidity on the temperature of the water, the length of the application, and, in the case of a douche, on the force with which it is applied. The reaction is assisted by voluntary movements and friction of the skin, and varies much with the health and strength of the individual and with his previous habits in respect of cold bathing. To those already accustomed to cold baths the initial shock is not unpleasant, and the reaction sets in much more easily.

Many physiological experiments have been made to explain scientifically what takes place when the whole body is exposed to cold. The pallor of the skin during the initial shock is due to the contraction of the superficial blood-vessels, which sets up a corresponding dilatation of the internal vessels of the body. As the blood is the great distributor of heat in the body, the central temperature, measured by a thermometer in the rectum, may rise slightly at first. The contraction of the superficial blood-vessels of the body must prevent excessive loss of heat until

heat-production is increased. Owing to this contraction of the superficial blood-vessels the general blood pressure rises and the heart's action is increased. When the reaction sets in the superficial vessels dilate, the flow of blood through the skin is much increased, and affects the sensory nerve terminations so as to give rise to a sense of warmth in the skin. Accompanying the reaction a thermometer in the rectum shows a slight lowering of the central temperature, which then gradually regains its initial level or slightly surpasses it.

The vascular phenomena consequent on the hydrotherapeutic application are clearly proved to be due mainly, if not entirely, to nervous vasomotor action; for, although the muscular walls of the arterioles, like other unstriped muscle, can certainly react to direct stimuli, the phenomena follow a stimulus too fleeting to act directly on the muscle-fibres (Hayem). The phenomena are not, to any considerable extent at least, due to the peripheral nervous mechanism, but to a reflex mechanism including the central nervous system: in animals they are absent from parts in which the nerves have been experimentally cut; and in the case of men the phenomena may be diminished or absent in paralysed and anæsthetic limbs. An attempt to trace out the "reflex arcs" concerned in the hydrotherapeutic reaction would take us too far away from practical medicine.

The respiratory phenomena observed after the application of cold water to the skin are also due to a nervous (reflex) action; they have been produced in animals rendered insensible by chloral (Roehrig). These phenomena consist in increased amplitude of the respiratory movements, with increased liberation of carbon dioxide and absorption of oxygen by the blood circulating through the pulmonary capillaries.

Increased combustion in the tissues is due to the need for increased heat-production to compensate for the heat given up to the cold water. Shivering must be regarded as part of the means whereby nature causes increased heat-production. Liebermeister first proved experimentally that heat-production was increased by the application of cold to the skin, and as in muscular exercise, this increased combustion causes an increase in the carbon dioxide given off by the lungs. When, owing to the continued application of cold, the muscular layer of the body becomes cooled, catabolism is temporarily diminished, but it is again increased when the reaction takes place.

The flow of urine is increased and the action of the bowels promoted, the latter probably being due partly to increased peristaltic action, partly to increased intestinal secretion. Increase of urea and diminution of uric acid are sometimes observed in the urine of patients under hydrotherapeutic treatment. The appetite is stimulated, the digestion of food aided, and the tonic effects on the nervous and muscular systems increase the desire for physical exertion and make work feel lighter.

If the cold application (douche or bath), instead of being general, be *local*, and especially if it be limited to an extremity, the general effects are less marked. Local applications have been shown, however, to cause

certain distant reactions. Thus, when iced water is applied to one hand both become colder, and both show a diminution in volume as measured by the plethysmograph. These phenomena are doubtless due to the diminution in the amount of their blood caused by contraction of their blood-vessels. Inverse phenomena, according to some observers, take place at a level of the body remote from that affected by the cold application; thus, during the application of a cold hip-bath, Winternitz has found that an augmentation in the volume of the arm takes place. These distant reactions, following on local applications, form an additional argument in favour of the reflex nature of the general "hydrotherapeutic reaction." If a so-called antiphlogistic action be desired, it is important that the local application of cold be continuous: Leiter's tubes are less easily displaced than icebags.

Warm-Water Treatment.—Whereas the chief ultimate effect of cold stimuli to the skin is tonic, that of warm stimuli is sedative. The effect of the warm treatment is not, however, exactly the opposite of that of the cold; indeed, all cutaneous stimuli, whether mechanical (by friction or massage), electrical (by faradic shocks), chemical (by counter-irritants), or thermic (cold or hot), show certain points of analogy.

Like cold applications, hot ones possibly produce an initial vaso-contraction; if so, this passes off quickly and gives place to vaso-dilatation, which lasts during the rest of the application, and then slowly passes off. This dilatation of the superficial vessels, with the subjective feeling of warmth, is the characteristic effect of hot applications. The superficial vaso-dilatation is associated with increase in the secretion of sweat and in the frequency of the respiratory movements. The whole constitutes the reaction of the body to heat, and thus the animal mechanism increases the loss of heat to counteract the heating effects of the application. Owing to superficial vaso-dilatation more heat radiates from the body; by increased sweating the loss of heat by evaporation is augmented; and by increased respiratory movements more heat is given off in the expired air and watery vapour.

In addition to the local sedative action of hot applications on the sensory nerves, as seen in the application of poultices and hot fomentations, there is a general sedative action exercised by heat when the application is general and sufficiently prolonged. This general sedative action is shown by diminished desire for exertion, and it is probably explained by the partial emptying of the deeper blood-vessels and slowing of the blood-streams which accompany the dilatation of the superficial vessels, and cause a certain anæmia of the viscera and brain.

If the loss of heat be partly prevented by immersing the whole body in a bath of hot water, the central temperature, as measured by a thermometer in the rectum, rises somewhat; but doubtless in such cases diminution of the heat-production in the body assists the loss of heat by respiration in order to prevent an undue rise of the body temperature.

Hot applications tend to produce constipation. This may, perhaps,

be due to diminished peristalsis, perhaps to a diminution in the intestinal secretion from the increased excretion of sweat.

The local applications of hot water, like local cold applications, but to a lesser degree, are said to cause certain distant reactions. Thus when one lower limb was heated, vaso-dilatation, increase in volume, and sweating were observed in the other lower limb.

Hot-air and vapour baths differ from hot-water baths chiefly in the temperatures at which they can be used, and in their action on the skin; the greatest amount of perspiration is obtained by hot-air baths.

The Internal Use of Water.—Plentiful drinking of water leads to increase in the watery secretions; besides the urine, the bile, saliva, pancreatic juice, and sweat appear to be increased; though if increased secretion of sweat be desired, it is generally stimulated by heat or bodily exercise. This increase in the watery constituents of the secretions is accompanied, for a time at least, by increased excretion of the waste products of tissue metabolism, which are "washed out" from the tissues and the blood itself. The effects of plain water taken internally form a considerable part of the results obtained from courses of mineral waters (see article on "Balneotherapy"), and the treatment may exercise a good influence in some cases of gout, urinary gravel, imperfect secretion of bile, and constipation from sluggish peristaltic action. Excessive water-drinking, on Priessnitz's original plan, may, however, lead to digestive troubles.

Diseases and Morbid Conditions Suitable for Hydrotherapeutic Treatment

Digestive Derangements.—Habitual constipation from atony of the bowels, often associated with a tendency to hæmorrhoids and "abdominal venosity," may sometimes be treated with cold baths and douches, and other stimulating methods, which increase the general nutrition of the tissues and the physical and psychical energy of the nervous system. In gastric atony similar treatment is useful according to the reactive powers of the individual. In cases of chronic dyspepsia with catarrh of the stomach, the common salt waters and alkaline sulphated waters (as at Carlsbad) are more frequently used and are usually preferable; but hydrotherapeutic treatment may be employed for the tonic after-treatment, or it may be employed with due care from the beginning as an adjuvant to the other treatment.

Muscular Pains and "Muscular Rheumatism."—Some of these cases may be treated with cold, some with hot baths, or with hot-air or vapour baths, according to the patient's power of reaction; they are often treated by warm or hot baths, followed by a cold shower-bath. The diaphoretic methods by packing with woollen blankets or wet sheets are often found to be useful, but they sometimes fail. In this class of cases the original supporters of hydrotherapeutic treatment considered their methods infallible, but this is by no means true. Invalids of this class should not be exposed to all weathers during the cure, and the access of cold air

to the wet body should not be risked. The course of treatment should not be too prolonged at one time, but may be repeated again after an interval of some months; the interval may advantageously be spent at sheltered sea-side localities, at moderate elevations, or at one of the gaseous thermal saline spas.

Gouty and Rheumatic Neuritis, and Neuralgia of the Sciatica Type.—Patients are often benefited by hot baths, and they are also often sent to thermal spas, such as Schlangenbad, Wildbad, Bath, Aix-les-Bains, Bourbonne. In the early acute stages rest is important, and pain is generally greatly relieved by local baths of hot water, vapour, or hot air (including electric light baths). In later, more chronic stages, vigorous douching, Scotch (alternating) douches, douche-massage, and massage associated with thermal treatment are useful.

Hepatic and Renal Colics, etc.—Hot baths may be of great service in hepatic and renal colics, probably by the relaxing action on unstriped muscle, and in helping the action of opiates. They may sometimes be of service in severe flatulent colic, in tenesmus, in retention of urine, etc.

Rheumatism, Rheumatoid Arthritis, and Gout.—In chronic rheumatic joint affections the patient is often too enfeebled for cold hydrotherapeutic treatment, but a hot bath (with the help, if necessary, of a crane-chair to lower the patient into the bath) may be useful in the treatment of such cases. In painful deforming rheumatism and rheumatoid arthritis of the small joints of the hands and feet, very hot-air (including electric light) baths, and hot-mud ("fango") applications are of great service. Mild cases of gout may derive benefit from the usual hydrotherapeutic treatment, in so far as it aims at invigorating the nervous system, and producing more complete oxidation of the downward products of tissue metabolism; the treatment should be associated with moderation in the amount of food, and especially in the use of stimulants. Local packing may induce attacks of gout, and indeed the hot-mustard foot-bath has been used for this purpose in cases of supposed "suppressed gout." The more severe forms of gout are too much complicated with general constitutional defects to encourage us in recommending cold-water treatment. Local hot-water, air, vapour, or mud baths are of much use for painful gonorrhœal rheumatism of the joints, fasciæ and tendon sheaths, and for certain cases of arthritis of obscure nature. For the stiffness and other chronic results of gonorrhœal rheumatism, and of traumatic articular affections, hot or alternating (Scotch) douches with passive movements and massage are of the greatest value.

Obesity.—The methodic use of sweating, followed by sufficient withdrawal of heat (by cold douching, swimming in cool water), so as to increase catabolism in the body, may be employed in addition to treatment by diet and exercise in the reduction of obesity. It must not be forgotten, however, that a course of Turkish baths by themselves, without the liberal application of cold water, generally tends rather to cause a gain in weight than a loss.

Catarrhal Attacks.—Weakness or over-sensitiveness of the skin, or

nerve terminations in the skin, may be the cause of frequently recurring attacks of diarrhœa, or of a tendency to catarrh of the respiratory mucous membrane; at all events, when this over-sensitiveness is present, cold is more likely to induce such attacks. Hydrotherapeutic methods, mildly stimulating at first, with gradually increasing energy, are here useful; unless, as in impeded convalescence, the reactive power is so reduced that gaseous thermal salt baths and mountain air are preferable. In some cases sea-air and sea-baths are most useful.

Chronic Affections of the Skin.—In local perspirations, some cases of pruritus, and chronic affections of the skin, hydrotherapeutic treatment in a modified form may be useful; it may also be used as an adjuvant in the treatment of syphilis. In some affections of the skin alkaline baths are of service, and bran-baths are used to allay cutaneous irritability. Chronic psoriasis and very chronic eczema have been treated by prolonged tepid baths, but in such cases a preliminary cutaneous reaction is probably always necessary before subsidence of the eruption.

Chronic Metallic Poisoning.—In some cases of this nature, if there is sufficient reactive power, cold-water treatment may be of as much good as the thermal sulphur treatment. The treatment will be aided by the abundant internal use of water, and if necessary by the administration of iodide of potassium, which is commonly supposed to assist in the removal of the poison from the tissues.

Hysteria, etc.—Hydrotherapy, pine-baths, and aromatic baths may sometimes be found useful in the treatment of hysteria and functional nervous affections, and in some cases of "diabetes insipidus." In all feeble and erethic subjects, however, treatment must be restricted at the commencement to the mildest processes. In organic nervous diseases hydrotherapy is not to be recommended, except in the form of hot baths, to relieve the lightning pains of tabes.

Catamenial Irregularities.—These are frequently treated at hydrotherapeutic establishments. Profuse menstruation may often be checked by the regular use of the cold hip-bath for three to five minutes. In cases where the menses are insufficient, warm hip-baths of ten to fifteen minutes' duration, combined in some cases with wrapping in a wet sheet, may often be found useful; dysmenorrhœa is likewise occasionally treated with advantage by the partial wet sheet or hot baths.

Anæmia.—In some conditions of slight anæmia hydrotherapy is useful, and a gradual increase in the hæmoglobin and number of the red blood corpuscles may be observed, not merely a temporary increase of corpuscles following general cold applications; the latter phenomenon may be explained as a mechanical result of the altered circulatory conditions induced by the cold. Of course special care must be observed in the treatment by cold water of feeble persons. The loss of heat can be counteracted by rest in bed, by wrapping the body after the application of cold, by preliminary moderate exercise, or by previously over-heating the body in the hot-air chamber, or by the alternate use of hot and cold water, as in the Scotch douche.

Rickets.—In some rickety, scrofulous, and other ill-nourished children regular bathing in rather cold salt or sea water may form a part of the treatment, provided that great care be taken to avoid a chill.

Pulmonary Tuberculosis.—Hydrotherapeutic methods, such as brief tepid or cold douches in the mornings, according to individual reactive powers, may be employed in some of the slighter cases for their tonic effects on the nervous and digestive systems. Indeed, a modified cold-water treatment constituted almost a part of the regular sanatorium routine under Brehmer and others. Hot-water and tepid sponging at bed-time are sometimes useful for the night sweats, which, however, are fortunately often obviated by modern open-air methods.

Infantile Convulsions, etc.—Hot baths of short duration, with or without the addition of mustard, are often employed for the immediate treatment of laryngismus stridulus and general convulsions in children. Hot baths also are sometimes used for adults in cases of puerperal eclampsia and uræmic convulsions, but in these cases some benefit is expected from their diaphoretic action as well as from their sedative influence on the cerebrum. Cold douches, or the continuous application of cold (by some form of "cap"), to the head are often of the utmost value in acute delirium; as, for example, in the course of the infectious fevers. Delirium and screaming are sometimes arrested almost at once by holding the patient's head over a pail at the bedside and pouring cold water over the head, beginning near it and slowly raising the can higher and higher.

Nephritis and Uræmia.—The wet pack, hot-water, hot-air, or vapour baths are sometimes of service by producing diaphoresis. When the patient has to remain in bed the application of the two latter baths requires especial care.

Enteric Fever and other Acute Infectious Diseases.—Of acute febrile diseases enteric fever is the one in which cold baths have been most practised. Brand's direction for the use of the cold bath is in general to take the rectal temperature every three hours; if it be 102·2° F. or more, the patient is to be placed in a cold bath of 64·4° F. to 68° F., and to be kept there until a slight shivering is observed, probably about a quarter of an hour. There are, however, many varieties of this treatment; many English physicians, following von Ziemssen, have preferred to place the patient in water at about 90° F., and to cool the bath gradually by the addition of cold water until the fever is reduced to about 101° F. Von Ziemssen's method is to cool the bath down within fifteen minutes from about 95° to 68° F., or, more correctly, from a temperature of about 5° C. below the patient's body temperature to 20° C. (68° F.); during the bath the skin is lightly rubbed, and in 20-30 minutes, or when shivering commences, the patient should be put back to bed. His temperature usually falls one or two more degrees after removal to bed, which should be warm and contain a hot bottle for the feet. In Liebermeister's plan the baths are given during the night, from 7 P.M. to 7 A.M., when there is a natural tendency for the temperature to fall, and not during the day,

unless the temperature is extraordinarily high. This plan of almost exclusively night bathing is certainly not practised generally. Bäumler of Freiburg has devoted much attention to the subject, and his routine methods deserve attention. On admission to his clinic the typhoid patient receives a cleansing bath if his general condition allows it. The axillary temperature is then taken every two hours during the day, and when it reaches 103·1° F., if there be no contra-indication, a bath at 82·4° F., or lower, but seldom under 75·3 F., is given, according to the age, sex, and strength of the patient. The individual reactive powers can be estimated by the first baths, and in the case of young, strong patients, who have not as yet become severely ill, a temperature of 68° F. is generally soon made use of. The bath lasts till the patient shows signs of getting cold, that is, for about ten minutes generally, sometimes more, sometimes only eight minutes. The patient's head rests on an air-cushion attached to the bath; his skin is chafed or rubbed (the abdomen being excepted), and the water is kept in motion as long as the bath lasts. After the bath a grave case is merely wrapped in a dry sheet and covered up, with a hot-water bottle at the feet, or more of them if required. Before the bath a little wine is given him, and after it sometimes warm bouillon. The patient usually soon falls into a peaceful sleep. In some cases (when the sensorium is much affected, or when there are respiratory complications from pulmonary catarrh with areas of collapse) Bäumler terminates the bath by a rapid cold affusion at 50° to 59° F. Sometimes the patient is likewise given a bath during the night. In our own ordinary hospital cases of late years the treatment adopted has been mainly on Bäumler's lines. It may be mentioned in this place that Dr. J. Barr has employed continuous immersion in a tank at 90° to 98° F. with apparently satisfactory results, but now that the beneficial action of baths is no longer believed to be a mere antipyretic effect, the continuous bath treatment is not likely to be tried again for typhoid and other fevers, though it may be still sometimes employed for certain surgical cases.

Cold affusions, cold sponging, the cold wet pack, the so-called "ice poultice," or other application of ice to the body, or the suspension of ice in vessels in a bed-cradle (so-called "ice cradle") within the bedclothes, have been used in milder cases for a similar purpose. Persistent fever in children may be conveniently reduced by filling wide-mouthed pickle-bottles with ice, wrapping each in flannel, and placing more or fewer of them about the patient—in the axillæ, against the flanks, or between the legs. Bottles may be added or removed from time to time as the thermometer may indicate. It must be remembered that part of the susceptibility of children to baths may be accounted for by the fact that the surface of the body, as compared to the volume, is greater in children than in adults. Generally, however, in ordinary typhoid fever cases methods like cold sponging are inferior substitutes for bathing. In regard to "ice cradles," etc., Dr. Caiger well observes: "From a purely antipyretic point of view, the 'cold-air bath,' as it might be termed, is excellent, but it is without any influence in stimulating the excretory

activity of the skin and kidneys, and thus promoting the eliminations of toxic products which is so marked an attribute of the cold bath."

The use of cold baths in enteric fever was introduced by F. Glénard in 1871 from Germany into France, and the writings of Glénard himself, and of R. Tripier and L. Bouveret, at Lyons, contributed largely towards the adoption of this method of treatment in France. Amongst the best known writings on the subject in the English language are those of Prof. Osler, Dr. J. Barr (Liverpool), Dr. F. E. Hare (Brisbane, Australia), Dr. J. C. Wilson (Philadelphia). Dr. W. Cayley, Sir W. H. Broadbent, and Dr. F. F. Caiger have likewise written in favour of the cold-bath treatment. The published statistics of results speak strongly in its favour. The prevalent opinion at present is that the fever of infectious diseases, although it may sometimes constitute a serious danger in itself, especially in typhoid fever and in hyperpyrexia cases, is, like the production in the body of antitoxins, part of the reaction of the organism towards invading microbes and their toxins, and to some extent may be regarded as a measure of the vital reaction, and thus indirectly of the severity of the infection. It is therefore unlikely that the beneficial effect of the bath treatment is due solely to its antipyretic action, and it is probable that the baths act as a tonic to the nervous system, and assist the organism to burn up and excrete the microbic toxins of the disease, and help it to get rid of its own excessive waste products (doubtless by increasing elimination through skin and kidneys). Moreover, it is not only really cold baths that have been found useful, but also tepid baths, though the latter are doubtless relatively cool when compared with the temperature of a feverish patient. It is possible that in delicate children and very feeble patients (see later paragraph) with infectious diseases hot baths may sometimes be of use. The bath treatment has been found useful not only against the fever, but also against the low delirium, subsultus tendinum, and other "nervous intoxication" symptoms of typhoid patients. Contra-indications are violent abdominal pain, collapse, intestinal hæmorrhage, and suspicion of peritonitis and perforation of the bowel. The patient's age and relative resistant powers must, of course, as already pointed out, be always taken into consideration.

The bath treatment has often been used successfully for acute infectious diseases other than enteric—in the "typhoid" symptoms sometimes occurring during the course of pneumonia, small-pox, erysipelas, scarlatina, etc., and good results have even been claimed in cases of delirium tremens. In pneumonia benefit is said to have been obtained also from hot baths (90° to 110° F.), but of this treatment we have no personal experience.

Hyperpyrexia.—In cases of hyperpyrexia, occurring in the course of acute rheumatism and other acute diseases, the advantage of the cold-water treatment over the internal use of antipyretic drugs is now generally admitted, and the methods of its use are well understood.

Collapse, especially in Children.—For children with collapse from diarrhœa and other causes hot baths may be used to diminish loss of heat and reduce the demands made on the enfeebled vital functions. A

similar use can be made of hot baths in ill-nourished children with broncho-pneumonia, in atonic pneumonia of feeble and aged persons, etc.

Burns, Cellulitis, etc.—The use of baths for these cases comes under the head of surgery.

Contra-Indications.—For the successful results of cold-water treatment it is essential that the organism be able to stand a certain amount of abstraction of heat; that it be capable of more or less energetic reaction, and that the digestive and assimilative organs be able to take up a fair amount of nourishing material to meet the increased catabolism. In cases of great debility after illness special care must be observed, and cold-water treatment is still more hazardous when, to the debility of illness, the weakness of childhood or old age is added. Cold morning baths are generally not advisable for thin persons inclined to cold extremities, especially if they are mentally overworked, of a nervous temperament, or with defective digestion. When cold-water treatment causes diarrhœa, urticaria, or hæmoglobinuria, it must be discontinued; and in chronic nephritis and any great degree of arteriosclerosis it is contra-indicated; the same holds good in cases of aneurysm, in those who have had one attack of cerebral hæmorrhage, or appear threatened with cerebral hæmorrhage, in all cases of heart disease, except in slight and well-compensated mitral valvular affections, in cases of hæmorrhage from the lungs or stomach, or after any severe hæmorrhage or tendency to collapse from any cause. When recommending hydrotherapeutic measures regard must be had to the general strength and reactive power of the individual patient as much as to the special trouble he complains of. The abundant use of liquids internally is injurious in cardiac and renal cases when there is a tendency to dilatation of the heart and failure of compensation. It is likewise to be avoided, at least with meals, in cases of obesity and gastric atony or dilatation.

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B. Balneotherapy; or, Treatment by the Internal and External Use of Mineral Waters

The term *Mineral Waters* is applied to those waters which are used in the treatment of disease, either internally or in the form of baths, on account of the saline or gaseous substances which they contain, or on account of their elevated temperature.

The science of the origin of these waters, and of the causes to which they owe their chemical composition and their temperature, is usually called *Balneology,* or in a wider sense *Hydrology*; and may be regarded as a part of Geology and Physical Geography: the art of using them in

the treatment of disease is *Balneotherapy*, and mineral waters are a part of Materia Medica. The additional terms *Crounotherapy* and *Crenology*, that is, treatment by wells (including the internal use of mineral waters), are not quite satisfactory, and are, moreover, unnecessary in addition to the words already mentioned.

This article is not intended as a regular treatise on Balneotherapy, but only as a survey of the uses of mineral waters in the treatment of disease. The external applications of mineral waters in the form of baths and douches, as practised at most of the spas, are, with few exceptions, similar in their effects to those of ordinary water at more or less elevated temperatures. We refer, therefore, to section A on *Hydrotherapy*; but we may mention here that at some of the spas various earthy matters, such as peat or moor earth and mud, are mixed with the water and used in the shape of general or local baths. Thus ferruginous "moor-baths" are much employed at Franzensbad, Marienbad, Carlsbad, Steben, Cudowa, Elster, and Pyrmont; sulphurous mud-baths are used at Nenndorf, Meinberg, and Wipfeld; salt mud-baths of various kinds are given at some inland brine springs (*e.g.* Ischl in Austria), at several places on the Baltic, and in Norway and Sweden, but especially at Odessa and localities on the Black Sea, along the northern shore of which the brine lakes ("limans") are situated from which the mud is obtained. In France, Saint-Amand and Dax are largely resorted to for their mud-baths. The hot mud ("fango") of Battaglia, Acqui, and other North Italian spas is much employed for local applications or poultices. In North America mud-baths are also employed at some places, as at Las Vegas Hot Springs in New Mexico.

We will divide the section on Balneotherapy into two parts:—

1. Description of mineral waters and their effects.
2. Therapeutic employment of mineral waters.

I. Description of Mineral Waters

The principal constituents of mineral waters are: Water, sodium, magnesium, calcium, and iron; combined with hydrochloric, sulphuric, carbonic, and hydrosulphuric acid. Other substances often present are: Arsenic, lithium, potassium, manganese, barium, bromine, iodine, alum, silica, and various organic matters; traces of copper, strontium, cobalt, nickel, and other metals have been detected. Free sulphuric acid is found in some of the sulphate of iron waters. The principal gases are: Oxygen, nitrogen, carbonic acid gas, and sulphuretted hydrogen; argon and helium occur in various simple thermal and thermal sulphur waters. These substances are derived partly from the surface soil, partly from the rocky strata through which the water deposited from the atmosphere has passed. The differences between the various mineral waters are due to the differences in the superficial soil and the rocks through which the water has passed

For convenience the mineral waters may be divided into groups, according to their temperatures, their chemical ingredients, their physiological or their therapeutical effects. Every classification is more or less imperfect, and an alphabetical arrangement would be the most easy; but this would entail frequent repetition, and thus require more space. We therefore attempt a somewhat mixed arrangement, based principally on the chemical constituents of the springs. It will, however, be evident that some springs contain so large an amount of several ingredients that they are entitled to a place in more than one group; and that others are named not after the substance which they contain in the largest amount, but after that which is held to be most potent. Those thermal waters which are almost devoid of solid substances are placed in a separate group. The following classification of eight groups may be employed:—

1. Simple Thermal Waters.
2. Common Salt, Muriated, or Chloride Waters.
3. Alkaline Waters.
4. Sulphated Saline Waters.
5. Iron or Chalybeate Waters.
6. Arsenic Waters.
7. Sulphur Waters.
8. Earthy or Calcareous Waters.[1]

The following description will only contain short sketches of the nature and action of the different groups of mineral waters and an enumeration of some of the representatives of these groups.

1. Simple Thermal Waters.—(Syn.: Wildbäder, indifferent thermal waters.) The waters of this group have a higher temperature than ordinary springs, varying between 80° F. and 150° F. or more; they are transparent, very soft, almost tasteless, of low specific gravity, very poor in solid and also in gaseous contents; in some there is a little more nitrogen than in ordinary waters; in others a little more oxygen.

Matlock, in Derbyshire, should be mentioned here, although the temperature of its waters is only 68° F. It lies in a beautiful valley, but the climate of Matlock itself cannot be called bracing.

Many other slightly mineralised warm waters, whose principal action is to be attributed to the temperature of the water, might be mentioned under this head, such as Acqui in Italy and the hot sulphur waters of the Pyrenees; while some of the spas mentioned in the accompanying table (p. 360), such as Leuk, Bormio, Bagnères-de-Bigorre, Badenweiler, Bath, and Aix-les-Bains, may be entitled to a place in other groups.

The very hot Algerian baths near Biskra, the "Fontaine chaude" (Hammam Salahin, Bath of the Saints), of a temperature of about 112° F.; Hammam Meskoutin, with waters of 170° F.; Hammam R'Irha, 158° F.; and others in Algeria, may be regarded as belonging to this group. In South Africa the thermal springs (120° F.) of Caledon, with the neighbouring "Caledon Sanatorium" (about 900 feet above sea-level), are useful for the residents of Cape Colony.

Some of the springs of the "Thermal Springs District" in New

[1] For all English Spas, see *The Climates and Baths of Great Britain*, by a Committee of the Roy. Med. and Chir. Society. London, Macmillan, 1895-1902.

Zealand may be placed here, though many, containing sodium chloride, sodium bicarbonate, sulphuretted hydrogen, etc., belong to other groups. The thermal springs of this district have temperatures ranging from 60° F. to 212° F. The New Zealand Government sanatorium and bathing establishment in connexion with them is at Rotorua, 990 feet above sea-level.

The United States of America are rich in simple thermal springs, some of which are in use, some in course of development. Some of the most important are: the "Hot Springs," "Warm Springs," and "Healing Springs" in Bath County (Virginia); and the "Hot Springs" in Arkansas, the "Calistoga Hot Springs" and the "Geysers" in California, the "Idaho Hot Springs" in Colorado, the "Hot Springs" in North Carolina, the "Warm Springs" in Georgia, the "Lebanon Springs" in Columbia County (New York), "Las Vegas Hot Springs" in New Mexico. It must be remembered that many waters most conveniently classed in the simple thermal group, in America, as in Europe and other parts of the world, contain traces of sulphuretted hydrogen. For the mineral waters of the United States the reader should refer to Dr. G. E. Walton's treatise (73), Dr. J. K. Crook's work (16), and Dr. G. Hinsdale's contributions in vols. iii., iv., and ix. of Solis Cohen's *System of Physiologic Therapeutics* (74).[1]

In the large cave of Monsummano in Italy hot vapour is disengaged from numerous surfaces of hot water and the patient walks about in it as in a spacious steam-bath. The benefit derived by Garibaldi brought new fame to Monsummano. Smaller, partly artificial excavations in the rocks of Battaglia, in the Euganean Hills of Upper Italy, are used in a similar way.

Enumeration.—The following table of some of the best-known waters of this group shows at a glance the two most important points, viz. the elevation above sea-level and the temperature of the springs.

[1] We must, however, object to some of the comparisons drawn by Dr. Hinsdale (*Journ. of Balneology*, July 1902) between American and European mineral waters. Thus Park's Spring in Carolina is placed by him as analogous to the Hunyadi-Janos Hungarian "bitter water," though the latter in its chief constituents (purgative sulphates) is nearly 700 times as rich as the former (which contains only about 0·05 per mille of the sulphates). Moreover, another spring in North Carolina is placed as analogous to both the Levico and the La Bourboule waters, which do not resemble each other excepting in so far that they both contain arsenic and may be placed in an arsenic.

[Table

Name of Spa.	Country	Approximate Elevation above Sea in feet.	Temperature of Springs in Fahrenheit.
Panticosa	Spain (Pyrenees)	5000	77° to 92°
Leuk (Loèche-les-Bains)	Switzerland	4600	102° to 122°
Bormio	Italy	4300	90° to 104°
Mont Dore	France	3440	104° to 116·6°
Wildbad Gastein	Eastern Alps	3300	95° to 104·8°
Pfæffers	Switzerland	2115	100°
Johannisbad	Bohemia	2000	86°
Bagnères-de-Bigorre	French Pyrenees	1850	90° to 95°
Ragatz	Switzerland	1700	96° to 98°
Badenweiler	Baden	1425	86° to 90·5°
Landeck	Prussian Silesia	1400	66° to 84·2°
Wildbad	Wurtemberg	1323	95° to 98·6°
Plombières	France	1300	65° to 156°
Luxeuil	France	1300	65° to 163°
Neuhaus	Styria	1200	95°
Liebenzell	Wurtemberg	1113	72° to 82°
Warmbrunn	Prussian Silesia	1100	97° to 104°
Tobelbad	Styria	1090	77° to 82°
Aix-les-Bains	Savoy	1060	86° to 120°
Buxton	England	1000	82°
Schlangenbad	Nassau	900	81·5° to 86°
Römerbad and Tuffer	Styria	700-800	81·5° to 86°
Néris	France	800	114° to 125°
Teplitz	Bohemia	650	95° to 120°
Lucca	Italy	500	100° to 120°
Dax	France	130	88° to 140°
Bath	England	100	100° to 120°
Idaho Hot Springs	Colorado	7500	85° to 115°
Las Vegas Hot Springs	New Mexico	6770	110° to 140°
Hudson Hot Springs	New Mexico	5000	142°
Boulder Hot Springs	Montana	4900	125° to 187°
Ferris Hot Springs	Montana	4500	122°
Hunter's Hot Springs	Montana	4480	148° to 168°
Hot Springs Warm Springs Healing Springs	Virginia	2300	85° to 108°
Castle Creek Hot Springs	Arizona	2300	115°
Hot Springs	North Carolina	1700-1800	96° to 104°
The Californian Geysers	California	1700	70° to 212°
Warm Springs	Georgia	1200	90°
Hot Springs	Arkansas	425	76° to 148°

Action.—The water of such springs, when taken internally, acts probably like any other pure, not hard, ordinary warm water of the same temperature. For this use we may refer the reader to the article on "Hydrotherapeutics," and will confine ourselves to the remark that warm water is more rapidly absorbed, and, by saving the expenditure of heat, makes less demand on the body. We are occasionally told by some patients, whose words are in our case-books, that a single tumblerful of the water of Gastein, or Wildbad, or Buxton, or Teplitz, or Bath has given rise to striking symptoms, such as the most severe headache, giddiness, inability to walk, sleeplessness, or, on the other hand, to rapid

removal of long-standing neuralgia, headache, sleeplessness, mental depression, anorexia, optic disturbances, etc. It is not impossible that these extraordinary effects, good as well as bad, which are quite out of proportion to the quality and quantity of the remedial agent, were due to imagination or suggestion.

Uses.—Courses of these drinking waters are useful in irritable conditions of the mucous membranes of the digestive and respiratory organs, in some cases of gastralgia, and in some forms of gout and rheumatism.

Bathing courses often act beneficially in allaying various forms of great sensitiveness and excitability of the nervous system, and are therefore often resorted to in cases of neuralgia, hyperæsthesia, and hysteria. Their reputation in painful cicatrices and rheumatism in the neighbourhood of old injuries is historical. In chronic rheumatism, in sciatica and allied affections, in some forms of gout and their remnants, these waters often assist and complete the cure, especially when combined with Swedish gymnastics and massage.

In the choice of the most suitable spa for individual cases the situation and climate of the spa, the elevation above sea-level, the quality of the bathing arrangements, and the accommodation must be considered; and not less so the attainments and skill of the medical men, and of the persons applying massage and Swedish gymnastics.

2. **Common Salt, Muriated, or Chloride Waters.**—Although common salt and other chlorides form the principal ingredients of these waters, many of them contain iron, carbonates of sodium, lithium, magnesium, and calcium; some also sulphates of sodium, magnesium, and calcium, others sulphides and sulphuretted hydrogen, and again others traces of bromine, iodine, and other substances. In some of these waters the action is no doubt modified by these admixtures, but as the effect of the chloride of sodium seems to predominate, they have been placed in this group. The difference of different springs is great, not only in the amount of common salt and other solid ingredients which they contain, but also in the presence of free carbonic acid in greater or smaller amount in some of them; and further in the temperature, as some are more or less hot, while the majority are cold. In a larger work it would perhaps be advantageous to make several subdivisions according to strength, according to temperature, according to the presence or absence of carbonic acid, and of other solid constituents; but in this survey we will only mention the more important common salt waters, dividing them according to their situation in different countries.

Enumeration.—The number of common salt waters in various countries is very great. England possesses concentrated salt waters or brines at Droitwich, Nantwich, Middlewich, and Ashby-de-la-Zouche. Droitwich, which has satisfactory arrangements and accommodation, is one of the best places for brine-baths. Moderate amounts of salt are contained in the waters of Woodhall, where they are combined with bromine and iodine in small quantities. Harrogate, situated in a bracing district of Yorkshire, the most flourishing of spas in England for drinking,

and to some degree also for bathing courses, has springs of varying strength in common salt, combined with sulphuretted hydrogen and sulphide of sodium. Llandrindod Wells (Wales) possesses similar springs, rather weaker, but still useful. Bridge of Allan, in Scotland, situated in a sheltered position, has an admixture of chloride of lime and sulphate of lime. Melksham (Wilts) deserves a place here as well as amongst the sulphated waters. At Leamington and Cheltenham the common salt is combined with relatively so much sulphates that these springs may be placed in the group of sulphated waters. England has no thermal saline waters.

In Germany and Austro-Hungary we may mention—Kissingen, Homburg, Soden (Taunus), Nauheim, Oeynhausen (Rehme-Oeynhausen), Kreuznach, Wiesbaden, Baden-Baden, Reichenhall, Ischl, Hall in the Tyrol, Hall in Würtemberg, Hall in Austria, Kreuth, Dürkheim, Niederbronn (Alsace), Krankenheil, Salzungen, Cannstatt, Cronthal, Aix-la-Chapelle (with sulphur), to which many others could be added. Germany does not possess brine-baths so concentrated as Droitwich, but it has the advantage of several waters rich in *carbonic acid*, as Kissingen, Homburg, Soden, Nauheim, and Oeynhausen; and again some with elevated temperatures, as Wiesbaden, Baden-Baden, Aix-la-Chapelle, Nauheim, and Oeynhausen.

France is rich in salt springs of elevated temperature: Bourbonne (Haute-Marne), Balaruc (Hérault), Bourbon l'Archambault (Allier), Bourbon-Lancy (Saône-et-Loire), Lamotte (Jura); Uriage (Isère) and St. Gervais (Savoie), both with sulphur; Châtel-Guyon (Puy-de-Dôme), with iron. Amongst the cold salt springs, Salins (Jura) and Brides-les-Bains deserve to be mentioned. France possesses concentrated brines in the waters of La Mouillère, near Besançon, and of Briscous, near Biarritz.

Switzerland possesses strong salt waters at Bex and Rheinfelden, the latter being as concentrated as the strongest English brines. In Italy one of the most popular salt spas is Monte Cattini in Tuscany; Castro Caro, likewise in Tuscany, is comparatively rich in iodine; at Salsomaggiore, in the province of Parma, which is largely resorted to and has excellent accommodation, the waters contain a bituminous material and are only used for external application (baths, douches) and for sprays and inhalation purposes. Ischia and Castellamare were used in ancient times.

Spain has in Caldas-de-Montbuy, in the province of Barcelona, a thermal salt water of great local reputation, and a weak one in Caldas-de-Malavella, in the province of Girone, remarkable for the large proportion of chloride of calcium and magnesium. Cestona-Guesalaga, another thermal muriated water, with weak mineralisation, is likewise of great local reputation in the north of Spain.

Caldas-de-Rainha, in Portugal, in a beautiful situation, is a most useful weak thermal salt spring, impregnated with sulphuretted hydrogen.

Russia is rich in brines, owing to the numerous salt-lakes ("limans"), especially in the neighbourhood of Odessa and along the northern coast of the Black Sea.

North America possesses St. Catherine's Wells (Ontario), Spring Lake Well (Michigan), Fruit Port Wells (Michigan), Ballston Spa (New York), and the much frequented Saratoga Springs (New York). The Mount Clemens Mineral Spring (Michigan) is a strong brine containing sulphuretted hydrogen.

Action.—Common salt is an important constituent of all our organs and tissues; it is an essential part of food, and cannot be dispensed with for any length of time. It plays a great part in the nutrition and metabolism of our body, but its exact action is still imperfectly understood. Owing to its easy diffusibility, a large portion of the salt taken in natural waters is absorbed at once in the stomach, while another part passes into the intestines. It stimulates the secreting apparatus of the stomach and intestines, the peristaltic action of the bowels, and the portal circulation. It seems to act specially on the mucous membranes, and to render their secretions less viscid. Voit thought that common salt increased the solubility and diffusibility of albumin, and his experiments seemed to corroborate those of Bischoff and Kaupp, showing that an increased supply of chloride of sodium caused an increase in the excretion of nitrogen through the urine. As many persons take at their meals a considerable quantity of salt in addition to that contained in the food itself, the extra amount taken in salt waters, say 100 to 300 grains at the outside, may seem unimportant; but if we remember that this extra amount, dissolved in water, is taken on an empty stomach during half an hour or an hour, and that the absorption ana diffusion is mostly aided by gentle exercise, it cannot be regarded as insignificant.

Carbonic acid in these waters, as in other mineral waters impregnated with it, seems to alleviate irritation of the sensitive nerves of the stomach, and by stimulating the minute capillaries and the secretion and peristaltic action of the stomach and intestines, to accelerate the passage of the waters from the stomach into the intestines, and to promote the action of the bowels.

In the form of *baths* chloride of sodium and the other chlorides act as stimulants on the nerves and blood-vessels of the skin, and this stimulus seems to be transmitted to the nerve centres and thus to influence the function of internal organs. A feeling of warmth is produced by a warm salt bath greater than is due to the actual elevation of temperature. The presence of carbonic acid in the water appears to heighten these effects. Actual absorption of chlorides does not occur, or, at all events, the quantity absorbed is so small that it may be left out of consideration.

Uses.—The common salt waters are much used in sluggish action of the bowels and stagnation in the branches of the portal vein, with the resulting troubles of dyspepsia, of congestion of the pelvic organs and hæmorrhoidal vessels and enlargement of the liver. In such conditions in spare persons, where emaciation is to be avoided, they are better than "bitter waters" (and also than the alkaline sulphated waters). They are also useful in catarrh of the stomach and intestines, and also in catarrhs of the respiratory organs, where they render the

secretion less viscid and promote expectoration. In chronic bronchitis their beneficial effect may be partly due to an indirect action on the right ventricle and to improvement in the contraction of the whole heart. Their use (especially that of the hot springs) in chronic rheumatism, in gouty persons, especially of the lean type, in sciatica, and some forms of neuritis is well known. Some of them have also long-standing reputation in scrofula, as Creuznach, Krankenheil, Reichenhall, Hall in Austria, Woodhall, and in the removal of chronic enlargement of the womb and remains of perimetritis. Many judicious gynæcologists maintain the good effects of these spas in uterine fibroids, although this is not generally admitted.

3. **Alkaline Waters.**—Waters of this class contain bicarbonate of sodium as a prominent constituent, and, in addition, a varying amount of free carbonic acid; but many of the waters contain chloride of sodium, and others sulphate of soda in so large a proportion that we are obliged to make three subdivisions:—(*a*) *Simple Alkaline Waters;* (*b*) *Muriated Alkaline Waters;* (*c*) *Sulphated Alkaline Waters.*

Enumeration of the principal spas:—(*a*) *Simple Alkaline Waters* are partly hot, partly cold. The European *hot* springs are represented by Vichy, in France, and Neuenahr, in Germany. The *cold* waters are Vals (Depart. Ardèche), Obersalzbrunn (Silesia), Le Boulou (Pyrenees), Fachingen (Nassau), Birresborn (Rhenish Prussia), Bilin (Bohemia); and a number of feebly mineralised waters which are used as *table* waters: Evian, Johannis, Apollinaris, Gerolstein, Geilnau, Giesshuebel, Soulzmatt. In North America there are the Bladon Springs in Alabama and the Sheldon Springs in Vermont, both rather weakly mineralised. The Geyser and Vichy Springs of Saratoga contain the bicarbonates of magnesium and calcium.

(*b*) *Muriated Alkaline Waters.*—The principal *hot* springs are Ems (Nassau); Royat (Auvergne), with some lithium, iron, and arsenic; La Bourboule (Auvergne), with arsenic; Châtel-Guyon (Auvergne); Saint-Nectaire (Auvergne); Szczawnica (Galicia). The *cold* springs are Luhatschowitz (Bohemia), Gleichenberg (Styria), Toennisstein (Rhenish Prussia), one of the Weilbach (Nassau) springs, and the table waters of Roisdorf, Rosbach, Kronthal, Taunusquelle, and Selters. In North America the St. Louis Spring in Michigan belongs to this class. The California Seltzer Springs and the Champion and Congress Springs of Saratoga contain carbonate of magnesium.

(*c*) *Sulphated Alkaline Waters.*—The different springs of Carlsbad (Bohemia) are all more or less hot; the weak springs of Bertrich (Rhenish Prussia) are lukewarm (87° F.); Marienbad (Bohemia), Franzensbad (Bohemia), Elster (Saxony), and Tarasp (Switzerland) are cold, as also Rohitsch (Styria) and a weak spring at Fuered (Hungary). The gaseous sulphated alkaline waters of the Royal Gorge Hot Springs (102° F.), near Canyon City (5360 feet above sea-level), amidst beautiful scenery in Colorado, somewhat resemble those of Carlsbad in Bohemia.

Action.—Like chloride of sodium, carbonate of sodium is an important

constituent of the human body, and plays a part in its metabolism. Liebig surmised that it acted as vehicle for the carbonic acid from the blood to the lungs. It has a great share in the secretion of saliva, bile, pancreatic juice, and the digestive processes. Introduced into the stomach, carbonate of soda neutralises the acidity of the gastric secretion, and acts as an antacid; it increases the flow of bile and renders it more fluid; it also renders the intestinal mucus less viscid, and acts as a diuretic. In large doses it is apt to cause emaciation; in small doses it rarely has this effect. The combination with common salt in the muriated alkaline waters further counteracts the emaciating and weakening tendency of the pure alkaline waters, besides which some of the action of common salt mentioned under that head is brought about. A greatly modified effect is exercised by the combination with sulphate of sodium in the sulphated alkaline waters. The laxative effect of the latter salt is predominant; it may be due to increased exosmosis or to stimulation of peristalsis, or to both combined. The increased movement in the intestinal walls leads to more rapid flow of blood in the branches of the portal vein and in the liver itself, and further assists in the fluidifying effects of the alkalis on the bile and intestinal mucus. By easing the portal circulation the work of a dilated heart is facilitated, and chronic pulmonary catarrh is relieved.

Uses.—Alkaline waters are serviceable in certain forms of dyspepsia where there is a tendency to excessive formation of acid in the stomach, and especially in those cases where this tendency is combined with catarrh of the stomach and intestines; but they are injurious in catarrhal conditions of the digestive organs with deficiency of acidity, as often occurs in anæmia, chlorosis, and convalescence from acute disease. The muriated alkaline waters act beneficially in chronic catarrh of the respiratory organs. The sulphated alkaline waters are often very helpful in atonic constipation with all its injurious effects on the blood, on the portal circulation, and consequent passive congestion of the liver; also in tendency to gall-stones and to uric acid gravel; in some forms of rheumatism and gout, and in the glycosuria of gouty and corpulent persons.

4. **Sulphated or Bitter Waters.**—This name is here applied to the waters containing as their active constituent the sulphates of magnesium and sodium. Some of them contain sufficient amounts of chloride of sodium to produce an alteration in their effects. The majority of these waters are used at home, not by residence at the spas.

Enumeration.—Franz Joseph, Hunyadi Janos, Æsculap, Apenta, and other "Hungarian Bitter Waters"; Rubinat, Condal, Carabana, and Villacabras, in Spain; Birmensdorf (Switzerland), Pullna (Bohemia), Sedlitz (Bohemia), Saidschutz (Bohemia), Montmirail (France), Friedrichshall (Saxe-Meiningen), Mergentheim (Würtemberg), Melksham (Wilts), the last three with a large proportion of chloride of sodium; Scarborough (Yorkshire), Leamington, and Cheltenham (*vide* Common Salt Waters).

In this class we may also mention Brides-les-Bains in Savoy, with hot

mixed sulphated muriated springs, containing the sulphates of sodium and calcium and chloride of sodium. These are the only European waters of this class which are principally taken not at a distance, but at the place itself, which is situated in a beautiful valley, south of the Mont Blanc chain.

In North America the following waters contain mixed sulphates and chlorides: the Crab Orchard Springs in Kentucky, and the so-called American Carlsbad Springs in Washington County, Illinois. They are weakly mineralised as compared to the "Hungarian Bitter Waters" of Europe.

Action.—In moderate doses the sulphated waters stimulate the mucous membrane of the digestive tract, and at the same time increase peristaltic action. In larger doses they cause watery motions. Their action is similar to that of the sulphated alkaline waters described in the preceding class.

Uses.—They are used in habitual constipation, with sluggish circulation in the portal vein and its branches, in passive congestion of the liver, and in excessive corpulency. They have the reputation of removing the latter by an accelerating influence on the retrogressive tissue-change. Whether this be so or not, no doubt they remove the alimentary substances from the intestines before all the nutrient material has been absorbed; they act therefore as abstractors, and, unless an increased amount of food is taken, the weight must decrease. We often hear that bitter waters are quite mild, certain, and easy aperients; this is the rule with many persons, but the exceptions to this rule are rather frequent. They act injuriously in most cases of chronic peritonitis and of the resulting adhesions, in ulcers of the stomach and intestines, and in cancerous affections of these organs.

We have sometimes heard that it is simpler to prescribe a certain amount of sulphates in substance and administer them dissolved in hot or cold water; but in our trials of this plan we have frequently found that a much larger dose of the salts thus prescribed was required in order to produce the same aperient effect as a dose of mineral water containing a smaller quantity of bitter salts. We have noticed this especially in using the more composite waters such as Friedrichshall, or Franz Joseph, or Hunyadi Janos, or the sulphated alkaline waters of the preceding class; in like manner, a larger quantity of the dried natural salts (say of Carlsbad salts) seems to be required than would correspond to the active quantity of the mineral waters at, say, one of the Carlsbad springs. It is probable that not all the substances contained in the mineral water are contained in the same conditions and combinations in the salts obtained from it; one point is evident, viz. that the free carbonic acid contained in some of the natural sulphated alkaline waters is lost in the salts obtained from the springs. The latter defect may often be corrected by taking the salts in one of the natural acidulated table waters, or in "salutaris," or in manufactured "soda water." Possibly, also, the preparation of the so-called "natural salts" is not always accurate, and

indeed some much employed salts may be intentionally modified, so as to furnish transparent crystallised instead of opaque amorphous salts.

5. **Iron or Chalybeate Waters.**—This term is applied to those springs in which the proportion of iron to the other ingredients is large enough to produce a therapeutic effect. A great many of the mineral waters enumerated in other classes contain iron; but the amount of other constituents is considered to predominate over the iron. Iron waters may be divided into a bicarbonate of iron group, and a less important sulphate of iron group. The bicarbonate of iron waters, which are most employed therapeutically, are rich in free carbonic acid gas, and the amonnt of the iron salt rarely exceeds eight centigrammes to the litre. The *bicarbonate of iron springs* may be divided into—(*a*) *pure iron waters* containing at the most only about one gramme of other solid constituents to the litre of water; and (*b*) *compound iron waters* which contain, besides the iron, a larger but still comparatively small amount of other substances, enough to alter somewhat the character without removing the predominant effect of iron. There is, however, no strict line of division between these groups.

Enumeration.—(*a*) *Pure or comparatively pure bicarbonate of iron waters.*—Schwalbach (Nassau), Spa (Belgium), Ceresole Reale in Piedmont, Koenigswarth (Bohemia), Orezza (Corsica), Brückenau (Bavaria), Tunbridge Wells (Kent); the last-mentioned water is poor in free carbonic acid gas. (*b*) *Compound bicarbonate of iron waters* contain, in addition to bicarbonate of iron, bicarbonates, sulphates, or chlorides of sodium, magnesium, or calcium.—Arapatak (Transylvania), the Stahlbrunnen and Luisenbrunnen at Homburg, Griesbach (Baden), Liebenstein (Thüringen), St. Moritz (Oberengadin), Santa Catarina (Northern Italy), Pyrmont (Waldeck), Recoaro (Northern Italy), Reinerz (Silesia), Godesberg (Rhenish Prussia), Bocklet (Bavaria), Innau (Würtemberg), Cudowa (Silesia), and Driburg (Westphalia). Amongst those containing an appreciable amount of sulphate of sodium are Rippoldsau (Baden), and the "Stahlquelle" at Franzensbad (Bohemia).

France possesses thermal iron springs containing bicarbonate of iron at Rennes-les-Bains (Aude), Sylvanès (Aveyron), and Lamalou (Hérault), which may perhaps be compared to the waters of Caledon in Cape Colony, to which we have already alluded under the simple thermal group.

Amongst the many European *sulphate of iron waters* may be mentioned the Flitwick Well (Bedfordshire), the Civillina water (Northern Italy), Ratzes and Mitterbad (Austrian Tyrol), and the waters of Levico and Roncegno (Austrian Tyrol); the two last are compound sulphate of iron and arsenic waters, and we shall again refer to them in the next (arsenic) group. The waters of Muskau (Silesia) and Alexisbad (Harz Mountains) contain both bicarbonate and sulphate of iron.

In North America, amongst the bicarbonate of iron waters are the following:—Bailey Springs (Alabama), Stafford Spring (Connecticut), Greencastle Springs (Indiana), Schooley's Mountain Springs (New Jersey), Montvale Springs (Tennessee), Rawley Springs (Virginia). Napa Soda

Springs (California), Geneva Lithia Spring (containing a little magnesium sulphate), Springdale Seltzer Springs of Colorado (containing a little sodium sulphate). Amongst the American sulphate of iron springs are the Oak Orchard Acid Springs, Bath Alum Springs, Stribling Springs, Bedford Alum Springs, Variety Springs.

Action.—The points accepted by the majority of medical men as to the effects of iron waters are :—Increased formation of blood; improved action of the circulatory apparatus, including the heart; better oxidation and heat-production; improvement in appetite and general nutrition. A small quantity only of iron is absorbed by the alimentary canal, and none by the skin. The baths of the pure iron springs owe their effects principally to the carbonic acid which they contain, and seem to act like ordinary water baths impregnated with carbonic acid.

Uses.—Iron waters are, in the minds of most people, the best remedy for anæmia; but their value in this respect is perhaps overrated. There are many cases of anæmia which are not improved, but aggravated, not only by pharmaceutical preparations of iron, but also by iron waters. Anæmia and chlorosis are often intimately connected with constipation and poisoning by ptomaines. In these cases pure iron waters are mostly injurious, while some of the chloride waters and sulphated waters, with or without small proportions of iron, are useful. Many other morbid conditions complicated with anæmia—for instance, malarial cachexia and some chronic skin diseases—are likewise rarely cured by pure iron waters, and this reminds one forcibly of the prescriptions of some very successful practitioners who combine good doses of sulphate of sodium or sulphate of magnesium with iron whenever they prescribed the latter.

There are, however, many forms of pure anæmia, and some conditions of neuralgia, sterility, impotency, and general debility complicated with anæmia, which are benefited by iron waters in drinking as well as bathing courses. In some cases of this kind the compound iron and arsenic waters are indicated (see next group).

It was pointed out under the head of simple thermal waters that the degree of elevation above sea-level must be regarded as an important point in the effects produced on the invalid. This applies to all the different spas, but especially to the chalybeate class. A course of waters, say of a month, at St. Moritz, or Ceresole Reale, or Santa Catarina, between 5000 and 6000 feet above sea-level, has a different effect on the constitution from that of similarly constituted waters at elevations below 1000 feet.

6. **Arsenic Waters.**—There are no pure arsenic waters, but the waters containing arsenic in appreciable amounts contain also either iron or saline substances. Arsenic is, however, such a powerful agent that we venture to place these waters together in a small separate group, in order to direct more attention to them. The group will probably be enlarged by further discoveries.

The strongest arsenic waters used at present are those of Roncegno and Levico, which contain sulphate of iron associated with minute

quantities of other metallic salts and with arsenic; they are both situated in the Tyrol, not far from Trento. They are both so strong that the doses required are small, and that they are advantageously diluted with warm water, or with one of the acidulous table waters, or with wine, and taken at or after meals in doses of one or two teaspoonfuls, increasing gradually to two tablespoonfuls. It is advisable to commence with small doses, and carefully to watch the effect, as in some persons they occasionally cause digestive derangements, such as diarrhœa; and in others constipation. There are good hotels both at Levico and Roncegno, but the waters are more used away from the spas themselves.

At Val Sinestra, in the Lower Engadine, there are springs containing arsenic in smaller quantity (one-fifth of the arsenic in the strong Levico water), combined with carbonate of iron and carbonate of sodium.

Ceresole Reale, in Piedmont, has, in addition to bicarbonate of iron, small quantities of arsenic; it is situated in a beautiful and bracing locality, and has good accommodation.

Uses.—These arsenical chalybeate waters are applicable to the same ailments as are the pure and compound iron waters, but specially deserve a trial in chronic skin affections with anæmia, and in lymphatic and glandular diseases, and in malarial cachexia.

La Bourboule, which was mentioned amongst the warm muriated alkaline waters, has such an appreciable amount of arsenic that it demands a preference over other muriated alkaline waters in chronic skin diseases, and may also assist in the treatment of chronic phthisis. It possesses, like the next-mentioned spa, the advantage of a somewhat elevated situation (2780 feet above sea-level).

Mont Dore, which was referred to in the simple thermal group, has a water containing less arsenic and other solid constituents than La Bourboule, but it has obtained a much greater reputation in the treatment of asthma. This is probably due in part to its higher elevation (3440 feet above sea-level), and in part to the very energetic use of inhalations; which, however, require careful management in delicate persons.

In North America there are various springs containing minute quantities of arsenic, particularly some of the Yellowstone National Park springs.

7. **Sulphur Waters.**—They contain either sulphide of sodium, calcium, potassium, or magnesium, or sulphuretted hydrogen in an appreciable and fairly constant proportion.

In some of the springs, as at Aix-les-Bains and Landeck, the quantity of sulphur is so small that they may be placed amongst the simple thermal waters.

In other sulphur waters the amount of chloride of sodium and other solid substances is so large that they may likewise find a place in the muriated or other groups; such, for instance, is the case with Harrogate, Llandrindod Wells, Aix-la-Chapelle (Germany), Uriage (France), Mehadia (Hungary), Caldas-de-Rainha (Portugal), Beck's Hot Sulphur Springs in Utah, the Columbia Springs in New York, and the Louisville Artesian

Well in Kentucky. Many sulphur springs are thermal, but some are cold.

Enumeration.—The best thermal sulphur waters are those of the French Pyrenees—Eaux-Bonnes, Eaux-Chaudes, Cauterets, Barèges, St. Sauveur, Bagnères-de-Luchon, Le Vernet, Amélie-les-Bains—which all contain the sulphur as sulphide of sodium, and are situated at fair elevations.

Other hot sulphur waters of great reputation are—Baden, Lavey, and Schinznach in Switzerland; Aix-les-Bains and Uriage in France; Aix-la-Chapelle and Burtscheid in Germany; Landeck in Silesia; Baden in Austria; Mehadia and Pystjan and others in Hungary; Acqui in Piedmont; Battaglia and Abano in the Euganean Mountains of Northern Italy; Panticosa in the Spanish Pyrenees; Trillo in the central part of Spain; Caldas-de-Rainha in Portugal; Hélouan in the desert near Cairo; some of these waters, such as Panticosa and Battaglia, can likewise be classed in the simple thermal group. Amongst the cold springs Harrogate is best known in England, Llandrindod Wells and Builth in Wales, Strathpeffer and Moffat in Scotland, Lisdoonvarna in Ireland; Challes, Enghien, and the Labassère waters at Bagnères-de-Bigorre in France; Eilsen, Nenndorf, Weilbach, Meinberg in Germany; Alveneu, Gurnigel, Stachelberg, and Heustrich in Switzerland.

In North America there are a great many sulphur waters, many of which, owing to their non-sulphurous constituents, can be distributed amongst other groups. Of the United States springs, according to A. C. Peale, the Cold Sulphur Springs of Virginia and Lane's Mineral Springs of California are specially rich in sulphuretted hydrogen gas. In British Columbia there are hot sulphur springs at Banff, on the eastern slope of the Rocky Mountains, in the Canadian Rocky Mountains National Park, 4500 feet above sea-level.

Action.—Sulphuretted hydrogen is absorbed by the skin and by the stomach; large quantities are poisonous by depressing the action of the heart, and by producing hæmolysis. It is, however, difficult to account for the alleged action of such small quantities as are taken up by the system during drinking and bathing courses. They are said to act as cholagogues, but this is not clearly demonstrated by experiments.

Uses.—They are used in chronic rheumatism and gout, but hot baths and hot-water drinking are likewise beneficial, and it is not certain that the presence of small quantities of sulphur adds much to the effect of hot water; the same may be said with regard to some chronic skin diseases. Chronic bronchial, laryngeal, and pharyngeal catarrhs are benefited; and often also hæmorrhoidal conditions. We have occasionally seen good effects in conditions of great irritability of the heart with palpitation. The ancient reputation of their good effects in poisoning with mercury or lead has become doubtful. Much has been written about the action of these waters in syphilis, but we must not forget that the successful physicians at these spas make most energetic use of mercury.

8. Earthy or Calcareous Waters.—Carbonate and sulphate of calcium and carbonate of magnesium are the principal constituents.

Enumeration.—Contrexéville, Vittel, Martigny-les-Bains, Bagnères-de-Bigorre, Pougues, and Cransac in France; Wildungen and Lippspringe in Germany; Urberoaga de Alzola in Spain; Chianciano (hot springs) in Central Italy; Weissenburg in Switzerland. In North America the best-known earthy springs are—Butterworth's Spring, Eaton Rapids Well, and Leslie Well in Michigan; the Old Sweet Springs in West Virginia, the Alleghany Springs in Virginia, and the Gettysburg Springs (weakly mineralised) in Pennsylvania. The French table waters Saint-Galmier and Condillac may also be placed in this class. Many of the waters mentioned in other classes contain much calcareous matter, for instance, Bath, Loèche, Bormio, and Lucca, classed amongst the simple thermal waters; and Baden in Austria, Baden in Switzerland, and Schinznach, classed among the sulphur waters.

Action.—Taken internally these waters exercise, through the carbonate of calcium, an antacid and soothing effect on the mucous membranes, and are at the same time slightly astringent and constipating, especially when they contain much sulphate of lime. In bathing courses their action is nearly the same as that of simple hot water.

Uses.—They are useful in dyspepsia, with irritability of the mucous membrane, acidity, and diarrhœa. Some of these waters possess a great reputation in proclivity to gravel and stone, and to chronic catarrh of the bladder. They are used also in biliary concretions, and in gouty conditions. Their good effects are probably due in a great degree to the circumstance that these waters can be taken in large quantities, and thus exercise a washing-out effect. In cases of actual stone of some size in the bladder, or in the kidney, the use of these waters is of doubtful value; the concretions may be actually increased by fresh deposits around them, but there can be no doubt that smaller concretions in the bladder and kidneys are often washed away by the free use of these waters. A speciality at some springs, especially at Loèche in Switzerland, is the treatment of chronic eczema, chronic psoriasis, and other chronic skin diseases, by hot baths prolonged over several hours, and this treatment is not rarely successful, at all events for a certain time; but relapses are rather common.

II. Therapeutic Employment of Mineral Waters

There is perhaps no section of medicine about which the ideas of the educated classes, and indeed of many members of our own profession, are so vague as about the effects of courses of mineral waters and baths, especially at foreign spas. On the one side we often hear that the good effects produced by spa treatment abroad are due not to the waters and baths, but to the concomitant influences, such as change of locality and habit of living; on the other, we hear that the waters alone are the

curative agents, and that they have, or ought to have, the same effect when taken at home. Both views are, however, narrow, and based on imperfect observation. The error of the former assertion is due to inferences from cases where the aberrations from health are not great, and are caused only by faults of home life, such as indulgence in food, irregular hours, social or business worry, excessive or unsuccessful work, acute or chronic mental shocks, want of exercise, and unhygienic arrangements. It is not quite so easy to show the error of the latter view, but it is equally real with regard to the majority of invalids. It is a great tax on the system to undergo courses of compound mineral waters. There are, it is true, strong persons with imperfect portal circulation, dyspepsia, hæmorrhoidal congestion, and inactive liver, who are able to right themselves by good purgative waters, and can take with advantage even courses of Carlsbad or Kissingen waters while continuing their usual diet and their daily work; but the majority of invalids, especially those with a delicate constitution or with a weak heart, do not possess the amount of vital force sufficient for the digestion of these waters, if at the same time their brain or their mind is taxed, if they have to go into society, and take long or large meals in close rooms. They often break down utterly if they attempt to do so. Even at country houses many people cannot disengage their minds to such a degree as to be able to bear these waters; and at the spas themselves it often happens that success is entirely spoiled by attention to letters from home, especially about business or family worries.

On the other hand, we have to deal with the opposite error, viz. the belief of many persons that the power of foreign waters is so great that they think they can remove large tumours, fatty, bony, or even carcinomatous; that they can unbend contracted limbs; that they can restore the muscles wasted from infantile paralysis, or the functions lost from senile decay. Incredible as this may appear to the educated medical man, such ideas persist in the high places of society. It is therefore very desirable that our profession should devote more attention to this important branch of treatment, and should diffuse general knowledge on the subject amongst the public. For this purpose a few lectures ought to be given regularly at our medical schools on balneotherapeutics, and also on climatotherapeutics, as a part of the course on Materia Medica or Therapeutics. We ought not to be deterred from such a course by the great difficulties besetting the subject, to which we can but briefly allude. While in our pharmaceutical remedies we have to deal with more or less fixed and simple substances, most of the mineral waters are compound; and, even if we know to some degree the action of the constituents severally, we often cannot accurately calculate the share which each of these substances plays in combination with the others, or their mutual interaction—points already alluded to in the description of the different classes of mineral waters. Ordinary treatment provides an approximately analogous state of affairs in the action of compound aperient pills or compound sedative draughts, but the difficulty is much

greater with compound mineral waters. Another point is that we prescribe the waters according to their most prominent ingredients, but we cannot be perfectly sure that the substances present in small quantities do not play a more important part in the action of the water as a whole than is generally conceded to them.

We must acknowledge that we have, as yet, no scientific basis for balneotherapeutics. Our position is still entirely empirical, based on the observation and experience of physicians and patients as to the effects of certain waters and cures, either at home or at the spas; but whilst admitting this as to the inexactness of our knowledge, we are obliged to allow that special bathing and drinking cures are most efficacious in many chronic morbid conditions, and cannot be replaced by any other modes of treatment (cf. Leichtenstern).

We will now endeavour to give a short sketch of the main points to be considered by the practitioner who is asked about mineral waters and baths. We must begin in every case with the question, whether balneotherapeutic treatment offers advantages over the ordinary medical treatment; and then consider whether this treatment ought to be carried out at home or abroad, and whether it is to be preceded or followed by pharmaceutical or other treatment, or combined with it. Having decided in favour of balneotherapeutic treatment, we must consider not only the nature of the disease, but all the conditions and habits of the individual before us, pecuniary, physical, and psychical; his constitution in general; his power of reaction; whether the different organs are healthy or not; whether they or some of them can take up increased work in order to relieve the diseased part; whether they are able or unable to respond to any unusual demand. Thus we shall learn whether vigorous therapeutic action is permitted; whether rough journeys and accommodation, colder climates and seasons can be borne; or whether gentle treatment is necessary, with easy journeys, warm seasons, mountain climates of moderate elevation, sheltered and sunny positions, and delicate food.

Knowledge of the chemical constitution of the waters alone is not sufficient for our selection of a health resort; we must know the accustomed methods of treatment at certain localities, the accommodation, the quality of food and the cooking, the climate, the social resources likely to be available, and, above all, the qualities of the local physician to be selected for the treatment of the case.

It must be obvious from these remarks that the same morbid condition may in different persons require different localities and even different classes of mineral waters; and, further, that diseases of different nature may be benefited at the same spa, by adapting the various bathing procedures and the doses and temperature of water to be drunk to the individual case, and by selecting, when there are different springs at the same place, the most suitable one. Often the treatment must be at first of a tentative nature, requiring the most careful watching by the local physician, and perhaps frequent alterations. In many cases it is

impossible to attack the principal complaint, and our efforts must be directed towards improving the general condition, by which means the diseased portion of the organism is very often drawn into the stream of general improvement.

Taking the different points just alluded to into consideration, every one will see how much depends on the *local physician*; and that it is not in the interest of the patient for the physician at home to prescribe, independently of the local doctor, the course of treatment to be adopted at the spa; though it is often advisable for him to make suggestions based on previous experience.

We will now sketch the applicability of waters to some morbid conditions, but must limit ourselves for want of space to a few states only.

1. **Tardy or imperfect convalescence** is the condition of many persons inquiring about waters, and the nature of these cases varies considerably. All have this in common, that they are in a state of instability; their balance is easily upset. Any increased demand on their nerve power, or digestive functions, may lead to illness; the nerves and blood-vessels of the skin are weak; and comparatively slight exposure leads to chill and to more or less grave results. We must therefore be careful to warn against fatiguing journeys, irregular or heavy meals, long, cold drives, defective clothing, and so forth. The majority do not require spa treatment; when they do, spas not too distant, with gentle treatment and good accommodation, in sheltered positions at medium elevations, should be recommended; or at first change of air alone without spa treatment. Later, iron waters or common salt waters are often useful. If there be still remains of disease, each such case will require special consideration.

In the exudations of perimetritis, for instance, after miscarriage or confinement, the common salt waters, such as Kreuznach, Kissingen, Woodhall, are useful.

If after rheumatic fever the skin remains weak, the joints painful, the heart dilated, with or without some valvular complication, the thermal gaseous saline waters of Nauheim, Oeynhausen, and Salins-Moutiers near Brides-les-Bains in the Tarantaise, or cold gaseous saline waters carefully warmed, such as Kissingen and Homburg, are of great value, sometimes assisted by Schott's resistance movements.

If tendency to diarrhœa be a prominent symptom, Plombières is often useful; if much neuralgia without organic cause, Schlangenbad: if chronic bronchial catarrh, the muriated or muriated alkaline waters of Soden, of Gleichenberg, of La Bourboule, or of Baden-Baden.

2. **Abdominal venosity** is a prominent feature of many chronic ailments, not only of the abdominal, but also of the circulatory and respiratory organs—of obesity, of drowsiness, of glycosuria, etc. The term used by the old German authors, *Abdominalplethora*, is very significant. It is often the cause of piles, of enlargement of the liver, of chronic pulmonary catarrh, and so on; and is generally part of a weak

organic fibre in the whole system, including the whole circulatory apparatus from the heart to the capillaries, the intestines, and the mucous membranes. Dietetic and hygienic management, the various forms of active and passive exercise, are pre-eminently useful, but these are greatly assisted and must sometimes be preceded by waters; here the alkaline sulphated, the "bitter waters," and the common salt waters are most useful, for an account of which the reader should refer to the first part of this article.

3. **Diseases of the Respiratory Organs.**—Climatotherapeutic treatment is, in the majority of cases, more important than waters, but the latter in many conditions may be a great help, and in others deserve the first place.

In chronic catarrh of the bronchial tubes the alkaline and muriated alkaline waters and the sulphur waters are beneficial; and when due to abdominal venosity, the recommendations of the previous section hold good. When the dilatation of the heart is the prominent feature, the gaseous muriated saline waters and baths, especially the thermal ones, assisted by the movements with resistance, are required. In other cases without special weakness of the heart, the muriated alkaline waters offer advantages, especially the thermal ones like Ems and Royat.

Emphysema comes more or less under the same head. Climatically, Gleichenberg in Styria and the spas of the Pyrenees are well adapted to these cases, and so is Ems in the earlier or later summer.

Chronic naso-pharyngitis, if not connected with adenoid growths, also requires alkaline muriated or sulphur waters, or the arsenical waters of Mont Dore and La Bourboule with inhalations.

Imperfect resolution of pneumonia needs climatic and skilled hygienic management, and sulphur and alkaline muriated waters, but with careful avoidance of exposure to the raw morning air while taking the early draughts.

Asthma depends on various causes, and accordingly requires various modes of treatment by drugs and water and climate, or is not amenable to any. The catarrhal form in fairly robust persons is often greatly relieved by the treatment at Mont Dore, a relief in which the elevated situation of the spa has a considerable share.

4. **Diseases of the Heart.**—We restrict ourselves to a few remarks. Many cases are not suited to long journeys and treatment by waters.

Fatty hearts or weak hearts in fat persons are mostly benefited by diet, combined with active and passive exercises and with sulphated alkaline and bitter waters. For dilated hearts associated with abdominal venosity, see sub-section 2.

In valvular affections with great anæmia iron waters are often useful; but in many cases aperient waters or pharmaceutical preparations, and Swedish gymnastics, must be combined with chalybeate waters.

In "weak" and moderately dilated hearts graduated walking and climbing exercise (Oertel) is better than baths; but if the dilatation be great, whether with or without valvular disease, the cautious use of the

baths of Nauheim, Oeynhausen, or Salins-Moutiers, assisted by movements with resistance, must precede the voluntary movements with climbing. In some cases treatment at home on the Nauheim plan must precede the journey abroad; and sometimes we must not be deterred from such measures by seemingly advanced symptoms.

Recent valvular affections resulting from rheumatic fever have already been mentioned in sub-section 1.

5. In **Anæmia** we must consider whether it is caused—(*a*) by direct loss of blood or albuminous and mucous discharges; (*b*) by constipation and impeded abdominal circulation; (*c*) by inability to take food, sleeplessness, mental shocks and worry, neuralgia, etc.; (*d*) by chronic diseases of the spleen, lymphatic tissues, and hæmopoietic system; or (*e*) by malarial infection and consequent affection of the spleen and liver. The more a case belongs to (*a*) the more likely is the effect of iron to be beneficial; and the physician has to decide whether chalybeate spa treatment offers advantages over pharmaceutical preparations combined with rest in the open air. In group (*b*) chloride of sodium waters are mostly preferable at first to pure steel waters; and a course of the latter, or of climatic treatment, or of both combined, may in many cases follow with advantage. In (*c*) climatic change alone with suitable mental surroundings is often more important than waters. In (*d*) the use of muriated and of arsenic waters may be tried; but they often fail, and ought at all events to be followed by long sea-side residence or sea-voyages. In (*e*) the muriated or alkaline sulphated waters at mountain localities ought to be combined with iron or arsenic, and followed by long residence at high elevations or occasionally sea-side places.

6. **Gravel and Stone.**—In the uric acid varieties the alkaline waters are generally prescribed, but great care is necessary not to allow the urine to become too alkaline, since this may lead to deposition of phosphates around a small uric acid stone. A better plan, in general, is to order the sulphated alkaline waters, especially the hot waters of Carlsbad, in the numerous cases where a certain amount of abdominal venosity and sluggish circulation of the liver are among the causes of gravel.

We have already mentioned that it is difficult to explain the great reputation of earthy waters in gravel, and that their effect is probably due to the administration of such waters in large quantities, so as to produce a washing-out effect, which probably would be obtained quite as well by the systematic drinking of large amounts of hot water on an empty stomach combined with an adequate regulation of diet, which in any case is to be regarded as a *conditio sine qua non*.

7. **Gout** occurs in widely-differing constitutions, varies widely in degree, and may or may not be complicated with various other morbid conditions. If we have to deal with persons of so-called "full habit"—with portal venosity, sluggish liver, and a urine of rather high specific gravity, loaded with urates and uric acid—the sulphated alkaline or mild bitter waters are indicated, especially Carlsbad, Marienbad, Tarasp, Franzensbad, Elster, Brides-les-Bains. All courses of the stronger waters

ought to be followed by a long rest with careful diet in good air before returning to the daily life; and this is pre-eminently the case with the courses just mentioned. If such a long rest be impossible, a less searching course ought to be recommended, such as, according to the nature of the case, at Homburg, Kissingen, Harrogate, Leamington, Royat, Contrexéville, La Bourboule, Wiesbaden, Baden-Baden, Aix-la-Chapelle, Uriage, Aix-les-Bains, or Bagnères-de-Luchon. A shorter rest is usually sufficient after these waters. In many delicate persons, especially if time be limited, the simple thermal waters are preferable—Buxton, Bath, Wildbad, Ragatz, Schlangenbad, Teplitz, Gastein. Numerous cases of gout, however, are not suitable for mineral water treatment, and will be found more amenable to pharmaceutical remedies, diet, and climate.

8. **Chronic Rheumatism.**—In cases associated with exudation round the joints, the hot thermal treatment is very useful; and it must frequently be combined with various forms of massage and Swedish gymnastics. The simple thermal waters, the hot sulphur waters, the hot muriated waters, can be employed with success. Chronic muscular rheumatism is amenable to similar treatment. In cases combined with affection of the heart, especially with dilatation, the tepid gaseous saline waters of the Nauheim type are preferable, associated with Schott's modification of Ling's system. Many cases are well suited to simple hydrotherapeutic treatment.

9. **Diabetes and Glycosuria.**—Not long ago some alkaline and sulphated alkaline waters, especially Vichy, Carlsbad, and Neuenahr, were thought to exert a specific influence on these complaints; but reason and experience have proved this view to be erroneous. It is quite true that in the milder forms of glycosuria courses of treatment at these spas improve the general health, and greatly diminish or temporarily remove the sugar from the urine. This, however, is due in the first place to the arrangement of diet, in the second to improvement of the digestive organs and functions by the use of the waters, and, thirdly, to the removal of the patients from the worries of life at home. In the frequent cases of chronic glycosuria in fat and gouty persons, sulphated alkaline waters are beneficial, and the more bracing the climate the better.

10. **Diseases of the Nervous System.**—Spa treatment is, as a rule, not applicable to mental diseases, although milder forms of hypochondriasis and depression, if they depend on chronic constipation or abdominal venosity, may be favourably influenced by the waters mentioned under the latter heading. Epilepsy and locomotor ataxy should be excluded, unless they depend on syphilis, which will be presently considered.

Nerve exhaustion and neurasthenia in their various forms and degrees may, according to the nature of the cases, be treated at chalybeate, thermal muriated saline, or simple tepid spas; but such treatment can only take a small share in a judicious general management, which must be pursued during a long period of time.

Neuralgic affections and the later stages of neuritis are often relieved by

spa treatment, if due to gout, anæmia, or to nerve exhaustion; and the selection of the spa must depend on these considerations. The relation of alcohol and syphilis to some of these cases must also be borne in mind.

11. **Affections of the Female Sexual Organs** are frequently treated at spas, although such treatment is not always required. Chronic congestion of the womb, especially in consequence of confinements and miscarriages, can be greatly benefited by the muriated saline, by the alkaline, and also by the simple and the sulphurous thermal waters. The removal of the exudations round the pelvic organs from perimetritis is often aided by the careful use of muriated waters. Many gynæcologists, both in this country and abroad, have great faith in the beneficial effect of these waters (especially those of Kreuznach) in fibro-myomas of the uterus.

12. **Syphilis** is regarded by many persons as one of the diseases which can be cured by the use of mineral waters; but all that can be said is that the use of other remedies may be assisted by them. It often happens that energetic mercurial treatment cannot be carried out under the usual conditions of home life, and that it is facilitated by the methodic employment of hot baths and vapour baths, and by the careful management of the manner of living, so as to avoid chills and other injurious influences. Thus, certain spas, like Aix-la-Chapelle and Uriage, have acquired a great reputation in the treatment of syphilitic affections, especially those of the secondary and tertiary stages. In this way many cases of affections of the skin, of the mucous membranes, of the muscles and organs of circulation, of the brain, spinal cord and nerves, epilepsy and tabes, with a syphilitic basis, are cured or benefited more or less permanently, or it may be only transitorily, by treatment at spas; but generally not by mere spa treatment. This applies both to acquired and to inherited syphilitic affections. As in home treatment, so also at spas, it is often found that serious affections on a syphilitic basis are no longer amenable to anti-syphilitic treatment, and that the latter does more harm than good. In such cases the means for the improvement of the general health are all that remain to us, and herein climate and spas may take again their humble share according to the nature of the cases.

We might mention a number of other morbid conditions which can be relieved by spa treatment, but for a mere survey the preceding classes of affections are probably sufficient. It is unnecessary to make suggestions about diet and manner of living, as each individual case ought to be considered on its own merits by the local physician, whose assistance, as we have already urged, is indispensable.

Seasons for Spa Treatment.—A few words as to the times of the year to be selected are perhaps not out of place. Climate and weather are important agents in spa treatment. Most delicate persons are better in summer than in winter; spa treatment, has, therefore, a greater chance of doing good in summer. Extreme heat, however, is to be avoided in most cases, and spas which are very hot in the middle of summer, such

as Wiesbaden, Ems, Aix-les-Bains, Vichy, Baden-Baden, Bath, ought therefore, as a rule, not to be visited in July and the beginning of August, but in the earlier and later parts of the summer. On the other hand, spas at high elevations, such as St. Moritz and Tarasp, ought to be recommended only between the middle of June and September. Few resorts are open earlier than May or later than September; but some of the hot springs, as Bath, Aix-la-Chapelle, Wiesbaden, Baden-Baden, Amélie-les-Bains, and Dax, are available during the whole of the year. It must be borne in mind, however, that much greater care is required when taking hot baths during the colder months, and that the exhilarating influence of fine weather is mostly wanting.

Duration of Courses of Spa Treatment.—Formerly it was the custom to have fixed periods for the treatment at different spas, say three, four, or five weeks; but in the light of increased knowledge we have learnt that it is in many instances impossible to fix at the outset the length of the course—just as it is often impossible to say, on prescribing iron or arsenic, that it is to be continued for two or three weeks and not longer. Much must depend on the effect which a course of spa treatment has on the individual case, and the local physician must decide not only on the doses, but also on the duration of the course. There are cases in which it is wise to give small doses for a long period of time, and others in which it is more advantageous to give large doses for short periods only. In some instances two courses are required in the same year, with a longer or shorter rest between them. Again, it frequently occurs that two courses of different waters ought to follow one another with a short interval between them: for instance, in a case of anæmia, with a sluggish portal system and passive congestion of the liver, it may be necessary to begin by a course of saline waters to unload the portal system, and afterwards to use chalybeate waters.

After-management.—The success of courses of mineral waters often depends entirely on the way in which the first three or six weeks following the treatment are employed. In almost all cases it is necessary to spend some time away from home at a good climatic resort, with careful diet and with open-air life, but without mental or bodily fatigue. It seems to be difficult for many people to grasp this, but we cannot too strongly advise our professional brethren to insist upon it. Some waters, like the simple thermal or thermal sulphur waters, especially when taken at bracing localities, require a shorter after-treatment than the more complicated and searching waters of Carlsbad, Marienbad, or Tarasp.

Every one who is acquainted with the "Weir Mitchell treatment" will admit that its author is correct in demanding after the termination of the treatment proper a further absence of six or eight weeks from the excitement and worry of home life; and some of us must have found that the neglect of this demand often destroys the good effect of the previous treatment. Similarly, after a serious course of waters the whole system is in many persons in an abnormal state of sensitiveness or unstableness, especially as regards the organs of digestion, circulation,

and, not least, the nervous system. Injurious influences, however slight, such as a chill, mental or bodily fatigue or excitement, or a mistake in diet, are apt to cause a fresh breakdown. We ought not to be influenced in our directions by the fact that some strong persons can do everything, even at or after Carlsbad, with impunity. Such cases form rare exceptions, not the rule.

Before concluding we must allude to an obvious mistake which is frequently committed. Many patients think that they do their duty towards themselves if they undergo a cure, and that they can resume their usual mode of living at the termination of the cure and after-cure. This is a great mistake in many instances. Persons who have lost their health, and have made a cure necessary by over-indulgence in food and stimulants, by want of exercise and injurious modes of living, ought to begin on their return home to live in a judicious way, since otherwise they are likely to lose all the benefit of the cure, and even aggravate their disease or diseases.

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PHYSICAL EXERCISES

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SYNOPSIS

Introduction

The health of an organism or of an individual organ depends upon the way in which its various functions are carried out. Be its anatomical condition ever so good, if it is not physiologically active, that structure will waste and finally disappear. Life itself depends not so much on anatomical structure as upon functional activity. Or this sentence may be translated as follows: the health and existence of a living being rest upon a proper exercise of all the cells and organs which enter into its formation. Further, the evolution of the various forms of animal and plant life is initiated by variations in their physiology, which are followed by changes in their anatomy. The inheritance of acquired characters is a coefficient of the physiological equation of living matter, not of the anatomical. It is the aim of physical exercises to improve the local and general conditions, and to adapt the various structures for the better performance of their functions. Throughout life exercise alone can improve and maintain the general and local tone of the body both in structure and function. The young naturally make the best subjects, as

their tissues are not so worn as those of older people. Exercises, when continued, can produce structural alterations in the body of adults such as those of the skeleton ascribed by Mr. Arbuthnot Lane to the various trades, or of the joint in the sternum, between the manubrium and gladiolus, found in working watchmakers of the old school. In youth and childhood the exercise of function will and does exert very great influence upon the anatomy of the body. It is the growth of the body which makes the anatomy of the child adapt itself to the various physiological forces to which it is exposed. The growing tissues of the child may be likened to gelatin being poured into a mould; the mould representing the physiological functions or exercises, and giving the ultimate shape to the jelly. In similar manner the child becomes moulded by what may be called its physiological environment. This natural disposition to change is instrumental both for good and evil. If a child is allowed to grow up badly, for example with poor chest development, the faulty positions will be permanently incorporated into its structure. In like manner good development gained in childhood is stamped on the body. At this point the medical man will step in. A deformity or fault has occurred; so long as it is present and growth continues it will be exaggerated, but if, whilst the child is young, the cause of the deformity is removed and curative measures adopted, the medical man has turned the powerful agency of natural growth to aid and perpetuate the good work he has begun. The period of childhood is the time for correcting physiological and anatomical errors, and for aiding those who are slow in developing. It is rather the surgeon than the physician who benefits most by natural growth. His operations, such as osteotomy and for hernia, are supplemented, and his whole work furthered and established, by natural growth.

To make the action of growth on a deformity quite clear a further explanation must be offered. The word deformity is to be read in its widest sense as an anatomical or physiological defect. Further, a deformity has at least two sides, the anatomical or structural and the physiological or functional. The contention is, that the latter is the more important in causing and perpetuating the deformity. By altering or modifying the functional manifestations it is possible to mould or remove the anatomical defect. For instance, in the functional deformation of the muscular tissue of the heart seen in weak action or imperfect compensation, the physician by means of rest can restore the strength anatomically, and afterwards by carefully graduated exercises can improve the condition physiologically. Or, to take a surgical instance, so long as the inguinal canal of a child contains a hernial protrusion, so long will it remain enlarged, that is to say, grow deformed anatomically; whilst the hernial protrusion is present this structural deformity is physiologically active. Let the surgeon remove the protrusion; the anatomical deformity becomes physiologically inactive, with the result that the inguinal canal is restored slowly to a more or less normal condition by subsequent growth. The surgeon, by

making the deformity physiologically inactive, has corrected the anatomical error of the inguinal canal.

Physiological exercises are useful under medical direction in the following ways :—

1. To develop the weakly or the overgrown.

2. To restore those convalescent, whether generally as from illness, or locally as from injury.

3. To correct during youth various deformities, especially those which detract from personal efficiency in life, such as congenital talipes and scoliosis.

4. To relieve certain general conditions such as debility and obesity.

5. To relieve local conditions after certain lung diseases; or certain cardiac, abdominal, or nervous affections.

6. To preserve the healthy tone of the body in those who by necessity or habit, virtue or vice, cannot do so in their ordinary lives.

7. To enable the body to counteract the baneful effects of educational efforts focussed on the mind. In this bodily education care should be paid chiefly to the chest.

8. As an educational measure for the mentally deficient.

Any consideration of the therapeutic uses of exercises is much curtailed when these measures are divorced from the younger and kindred subject, massage, which is a name given to the milder forms of passive exercise.

The Science and Art of Physical Exercises.—Like many other forms of special treatment physical exercises are open to abuse when their practice falls into the hands of unworthy, or of worthy but ignorant, persons. Such is too often the fate of certain departments of the science of healing, because in their practice demand is made for more faith than intelligence on the part of the patient, who is not infrequently a member of a very credulous and ignorant community. It is only by results, which in many instances they but partially understand, that the laity judge us. The methods of instruction by physical exercises can be easily and rapidly learnt by any one possessed of the average modicum of common sense. For the art, to see it carried out is of infinitely more value than any reading. Unfortunately, much of the literature on the subject is worthless, the erudition of the authors being represented by the use of a few anatomical terms. One would thus draw a fairly sharp line between the art and the science. The former can be quite adequately performed by those who do not know the "whys and wherefores" of their methods; the latter is the work of the skilled physician or surgeon, and it is his duty to supervise the proceedings and results of the former.

I. The Physiology of Exercise

1. Symmetry of Function.—A living particle, no matter how simple, differs from inorganic matter in the intrinsic power of altering its

composition. In the lower organisms this faculty of elaboration of structure is confined to the absorption of nutriment and the excretion of waste products.. If its evolution could be watched, an organism would soon be found to be undergoing alteration and adaptation for the better performance of this interchange with the surrounding media. In other words, by the exercise of its functions the organism has improved its conditions of life. The repeated performance of its functions, or its physiological activity, leads to the evolution of anatomical changes, such as the development of special organs for the various activities. What applies to the lowly organisms also applies to the higher and more complex being man. Man differs from a lowly organism in the infinite complexity of his anatomy and physiology. Unfortunately, if but one function is in abeyance or out of gear, the animal is below its natural and proper condition, and herein appears the idea of health—that in health all functions should be working harmoniously together—physiological symmetry. For its attainment one must take care to develop or restore perfect harmony in the exercise of our different functions. The man who develops one function out of proportion to the others does so at the expense of these. How commonly we meet with men all muscle and digestion, and with little mind ; and others all mind, but with an ailing body. By the actions of physical exercises, it is possible for us to exert profound influences on the body and health generally. There is a further and even more important application of the uses of physical exercises. The growth and development of a unit of the human race continue for many years after birth. During this plastic period of childhood we can watch over and influence the full symmetrical and harmonious development of the functions, applying correctives when observation shows them to be necessary. How far it is to be carried out must be carefully considered. For a man is not fit for the work of life if he is turned out from boyhood a perfect, symmetrically developed, and harmonious mass of living tissue, without predilections or tastes in any direction. This is not so difficult to avoid in the upper grades of society ; for, whether by inheritance or not, the young soon show the lines on which their main interests run. Very shortly they ascertain that it is impossible for any one of them to excel in everything. In consequence, they focus their energies upon one or more branches of the work of life, and strive to excel in that. This is not only applicable to the mind but also to the body. This specialisation of body as well as of mind is not to be discouraged when once both are fully developed and matured, or nearly so. Specialisation is the primary factor of future evolution. It is in physiology or the exercise of function, rather than in anatomy, that the key to evolution lies. More than this, one would look to the key of the processes of inheritance in the physiological rather than the anatomical variations, the latter being the slowly acquired results of the inheritance of the former. There has been much investigation on the inheritance of anatomical, but very little on that of physiological variations.

There is a limit set by nature to these variations or specialisations. If the specialisation of one function becomes inharmonious or asymmetrical, that is to say, at variance with the others, the organism suffers. In watching over the development of the young these general principles should be borne in mind. To develop the muscles at the expense of the other tissues to the degree seen in the strong men of public exhibitions is distinctly pathological. Similarly, those who have the care of growing youths would do very wrong to encourage an analogous asymmetrical growth of the mind or of the digestion. But these principles can be carried out into further details. One set of muscles, such as the legs, must not be allowed to become developed out of proportion, say, to the chest; and yet how often is this the case. How many young men just miss being great athletes in mind or body. There is a magnificent Hercules of a man rowing, but notice how his chest labours and his colour changes! The coach says that he is a powerful oar, but has no staying power or pluck. This is an example of the over-development of muscles combined with comparatively deficient development of the lungs and heart. It would be very interesting to see some of the professional strong men attempt to run half a mile.

A man may specialise as he pleases in any form of gymnastics or athletics, mental or bodily, so long as a judicious balance is maintained between the various functions of the body. Good respiration, good circulation, good digestion, good, but not extreme nervous activity, are the desiderata. A woman's scope in athletics and knowledge is curtailed by the necessity of her maintaining physiological symmetry or harmony of these with her function of child-bearing. In the past her activities have been restricted to this and to household duties, whereby a physiological asymmetry or discord arose in the opposite sense. Of recent years athletics and higher education have altered women's condition for the better, and in process of time will produce still further changes.

2. **The Effects of Contraction on the Muscle.**—When a muscle contracts it becomes shorter, broader, thicker, and harder, and the blood flows more quickly through it. In the process of muscular contraction the highly complex molecule of a chemical compound is broken up, and the energy so set free appears in various physical forms, thermal, electrical, chemical, besides the physiological contraction. The fibres which compose the muscle, having lost energy in this way, renew their supplies from the materials brought them by the arterial blood, and at the same time rid themselves of the waste products of the "chemical explosion" by giving them up to the blood in the veins. Thus, muscular activity results in the incessant change of some of the essential elements of the muscle-cell, which is maintained in a state of efficiency proportionate to its use. Both the number and the size of the fibres are said to be increased by exercise.

3. **General Effects of Muscular Exercise.**—When a muscle contracts it absorbs oxygen from the blood, and yields up to it carbon dioxide. In addition other chemical changes occur of which little is

known. Suffice it to say, that when energy is set free in a muscle, the blood while at that spot becomes altered, and, as a consequence, stimulates the important centres in the medulla oblongata; or the stimulation may be accomplished by afferent impulses from the right side of the heart. By these means respiration is quickened and deepened, the muscles concerned acting more vigorously. The blood is more thoroughly oxygenated and freed from waste products by the increased respiratory movements than it ordinarily is. The cardiac centre in the medulla is also stimulated and causes more frequent, efficient, and forcible heart-beats. Two more results of exercise will be specifically mentioned. Muscular contractions or explosions necessitate considerable loss of energy, or explosive material, which must be replaced by the ingestion of food, and is provided for by an increase of appetite, and digestion and absorption are improved. Secondly, the muscular contraction gives rise to the evolution of heat, as shown by the slight and transient rise of temperature after exercise. By the action of the thermolytic and vasomotor centres heat is lost, very largely by means of the activity of the skin, the evaporation of sweat cooling the body.

In short, exercise stimulates the activities of the respiratory, vascular, nervous, digestive, and excretory systems.

4. **The Importance of Position during Exercises.**—In every muscle, even when at rest, there is a certain amount of contraction, which is dependent on some tonic or continuous nervous action; consequently, when it contracts there is no "slack" to take in. Paralysed muscles have, to a large extent, lost this "muscular tone." About midway between the tonic condition of a healthy and the more or less atonic state of a paralysed muscle, are the flabby muscles of the sickly and under-developed; the flabbiness being dependent upon a poor tone of the muscle and of its nervous centre. Exercise increases the healthy tone of the muscle, and presumably also of its controlling nerve centre. The consequences of this increased tone are of importance. If antagonistic sets of muscles are unequally and therefore inharmoniously exercised, the increased tone of the more active group of muscles will cause a corresponding contraction when the part is at rest. For instance, a man whose daily work necessitates grasping something, such as an oar, will have over-developed flexor muscles, and his fingers will be curved when at rest. A further change will also occur, to which Mr. Arbuthnot Lane (13) has specially directed attention. Continuous or frequently repeated action of the muscles when in one position will produce such changes in the ligaments and, later, in the bones themselves as will make, or tend to make, that position permanent. For instance, the coal-heaver, from carrying heavy weights on his bent back, develops a very powerful set of dorsal muscles, but in spite of the presence of these huge muscles he cannot straighten his back, since the concurrent ligamentous and bony changes prevent it. In the case of growing bones, or of bones softened by some such

disease as rickets, mollities ossium, and so forth, the deformities will occur much more easily. This cannot be expressed better than in Mr. Arbuthnot Lane's words, "the skeleton is practically the crystallisation (of the action) of the lines of force" (14). When these bony deformities have occurred in the young, future growth and exercises may correct them; but they are always the most difficult part of any deformity to get rid of.

This subject has been gone into thus fully in order to emphasise the great importance of a proper position during the exercises. If the position is faulty—for instance, if "pulley-exercise" is done with the dorsal spine bent forward, the ribs depressed and the chest flat, the muscles which are developed and hypertrophied by that very exercise will tend to render the position assumed permanent. As will be shown in the section dealing with the importance of exercise in children, natural growth tends in exactly the same direction, so that a deformity if allowed to persist will become permanent. It is, therefore, of paramount importance that a good instructor should attend to this subject of position. The fault is chiefly to be feared in class-work, where it may remain unnoticed, or perhaps, from laziness or weakness, the child will only maintain the good position when the instructor is near. Careful inspection should be made of the individual members of a class during its work by some one other than the instructor, and changes should be made according to his observations. All exercise, bodily and mental, during childhood, should be most carefully watched; and if not all, at least the weaker children should receive individual attention and instruction wherever possible.

5. The Physiological Load and the Personal Equation for Exercise.—For every muscle or group of muscles there is a load under which it can do its greatest amount of work. This weight is called the physiological load, and varies in amount for each muscle. What is true for a muscle and a group of muscles is true for a limb, and also for each individual. Every one has his physiological load, his personal equation for exercise, which can only be ascertained by experience and experiment. The element of time affects the amount of this load very practically. For instance, in a given time a youth may do his greatest amount of work with a weight x. But for a longer time x will not yield the most work, though some lighter weight will. The proper number of pounds or kilogrammes varies with every individual, and must be most carefully attended to by the overseer and instructor. A careful watch must be made that the weaker members are not over-weighted, and that the stronger, who perhaps say nothing from laziness, are not under-weighted.

6. The Physiology of the Chest.—In early life our minds are carefully instructed and trained by highly educated men; but our bodies are allowed to develop according to the inclinations of the owners. Exercise is encouraged by all authorities, but the use made of the opportunities supplied rests with the individual, who will utilise it or shirk it

according to fancy. The results of the lack of good physical development can be easily and most satisfactorily estimated by the condition of the chest and the carriage of the body. Let it be clearly understood that although poor development of the chest always accompanies poor physical development of the body, a chest, poor as compared with the good muscular limbs, is frequent in the strong and the athletic. When such is the case, the larger the muscles the worse for the man. Let a skilled observer comment on almost any gathering of men and women. In many of them poor physique is evident in the flat chest, the nearly vertical sternum, the depressed ribs, the hollows above and below the clavicles, the round shoulders, the stooping back, and prominent scapulæ. Accompanying this condition of the thorax, and especially in the mature or prematurely old, the lower part of the abdomen becomes prominent, and is frequently accompanied by mental depression, bodily feebleness and indigestion, and a sluggish condition of the bowels and liver. Examination of such a chest with calipers or a tape during inspiration reveals very little thoracic movement with respiration, which is almost entirely abdominal. If only more trouble were taken in the instruction of our bodies, and particularly in the development of our chests, the time thus subtracted from that usually devoted to intellectual pursuits would be amply repaid by the better character of the work done. The whole race, particularly the middle and upper classes, would be much improved. The position of the thorax just described, with little or no movement on respiration, leads to stagnation of air in the apices, and to the form of chest favourable to the ravages of tuberculosis.

FIG. 1.—Figure of a poorly developed girl, showing the position of rest assumed in standing by feeble subjects. The vertical sternum, rounded shoulders, and the protruding abdomen should be noted.

It is well recognised that the brain is the seat of the mental activity, and that its development is an essential factor in the acquisition of knowledge and the power of thought. For bodily exercise there must be muscles and limbs to work, and for their smooth, good working, efficient action of the heart and of the lungs is all important. Both these organs are in the chest, so that, for good physical development of the body, there must be full and adequate action of the chest. Attention should, therefore, be paid to the chest whilst there is yet time, that is

to say, during youth; thus the busy man will have a chest with good expansion, which will enable him to put to the best possible use the limited time he has for leisure.

A short consideration of the physiology of the chest in exercise will make obvious the supreme importance of its development in youth. In the first place, the chest is a large cage with bony and muscular walls, capable of expansion and contraction. Its influence is exerted along five main lines. The first is the heart, then the lungs; thirdly, the aspiration of blood from the great veins; fourthly, the excursions of the diaphragm; and, lastly, the effects on the bony cage itself.

(*a*) *The Heart.*—At times the chest must be fixed to enable the muscles, especially those of the arms, to obtain a good mechanical pull; for instance, when the blade of an oar dips into the water and the oarsman "catches his beginning." This fixation of the chest has a disadvantageous effect upon the work of the heart. It prevents the free return to the chest of the blood in the great veins and produces passive engorgement, shown in the swollen veins on the head and neck of a wrestler. This engorgement does but little harm in itself, but the conditions are very different when there is in addition a rapidly-beating heart. At the time of this venous obstruction the right auricle is inadequately filled with blood, which it has to pass on at the next beat. It is the first of the heart chambers to experience this. At the next beat, when the chest is no longer the fixed point for the arms to pull upon, the right auricle and ventricle will become rather over-distended, just as they were previously imperfectly full. In another beat or so comes the powerful rapid expansion of the chest for inspiration, venous blood will be sucked forcibly into the auricle, which, together with the ventricle, will be much distended. In exercise, such as rowing, the heart has to adapt itself to receive and pass on rapidly varying quantities of blood. Hence the turbulent action of the heart seen in rowing men. Again, during exercise the normal relation between respiration and pulse is altered. In the normal person during rest it is between 1 to 4 and 1 to 5. In a man rowing at 30 strokes to the minute it will be between 1 to 3 and 1 to 4. The heart not only has to accustom itself to the increased work thrown upon it, but also to the altered rhythm and to quantities of blood which vary in amount at almost every beat! It is no wonder men find that it is not the amount of work done, but the rate of the stroke, which causes them most distress. Dr. D. B. Lees has said of the dyspnœa of muscular exertion: "Is not this due to the arrival of venous blood in the right side of the heart more rapidly than the ventricle is competent to pass it on into the lungs? Hence the tension in the right ventricle rises, the muscular walls tend to dilate, and a stimulus probably ascends to the respiratory centre, whereby more rapid and deeper inspirations expand the pulmonary channels and so relieve the labouring ventricle. Is not the management of the breath, which is the main part of the training for athletic exercises, simply an education of the right ventricle?"

(*b*) *The Lungs.*—This quotation from Dr. Lees broaches the second section of the physiology of the chest as regards exercise. He says that the deeper, quicker, and more powerful inspirations, by opening up the capillary vessels of the lungs, allow the surcharged right ventricle to relieve itself more freely. At the same time, the exchange of gases between the air and the blood will take place more freely, the latter becoming better oxygenated and freer from the by-products of metabolism. But for these processes to be of value, it is necessary that there should be full expansion of the chest, and a good volume of tidal air inhaled and exhaled at each respiration. Many men fail to become great athletes because they have never had any instruction in the development of their chests. The more the development of the muscles the greater will be the waste products of their contractions, and the more will the comparatively inadequate expansion of their chests fail to give relief. If the spring-time of youth has passed little further can be done, and the tide soon sets against them in the stream of competition. The occupants of the thwarts in a racing boat—4, 5, and 6 especially—are frequently fine men with big chests, the expansion of which is, however, inadequate for their muscular development, and therefore cannot, so to speak, clear the right side of their hearts.

(*c*) *Aspiration of Blood from the great Veins.*—The chest is a great aspirator during inspiration, the pumping action of breathing being comparable to that of a second heart. Air is inspired by being sucked into the chest by the descent of the diaphragm. But it is not the only fluid exposed to this forcible suction; the blood in the large thin-walled veins and the contents of the lymph-vessels are also affected. It is of considerable interest that the diaphragm, which creates the negative pressure of inspiration in the chest, also empties the receptaculum chyli.

Reference has already been made to the fixation of the chest involved in holding the breath during violent exertion. Persons with deficient chest expansion are unfit for great and protracted efforts. The products of metabolism cannot be thoroughly removed, and therefore accumulate in the system. The deficient aspiration of the venous blood into the chest prevents its rapid purification, although the heart in its efforts to give relief to the system increases the rapidity of its beat to a great or even to an alarming degree. The association of poor chest expansion with rapid cardiac action on exertion can be verified wherever young men take exercise.

Though it could hardly be said that deficient respiratory movements cause varicose veins, imperfect expansion must be regarded as an important disposing condition. It is certain that such persons are most frequently the subjects of varicose veins, and that many of them are much relieved by respiratory exercises. A certain number of those who have led sedentary lives and suffer from hæmorrhoids, will be relieved or cured by means of exercises and attention to the diet and bowels.

Let it be remembered that the heart is developed and adapted for ordinary quiet work. In consequence, during exercise its action is

inadequate unless assisted by movements of the chest. If the expansion of the chest is limited by poor development or emphysema the individual is unfit for hard work.

(*d*) *The Excursions of the Diaphragm.*—Full respiratory movements do a great deal towards maintaining the abdominal viscera in a healthy state of activity. The periodical filling and emptying of the contents of the receptaculum chyli at each inspiration have been mentioned. The suction of blood from the inferior vena cava will temporarily deplete the liver, thus relieving the pressure in the portal system. At the same time the abdominal muscles are exercised, and the figures of many people past middle age much improved. The waist measurement can be considerably lessened, so that comfort and pleasure can be taken again in walking and outdoor pursuits.

(*e*) *Effects on the Thorax.*—Finally, the influence on the bones, muscles, and ligaments which form the thoracic cage must be considered. All these structures adapt themselves to the amount of work done, and to the position in which this work is carried out. If the chest is held habitually flat and fuller expansion never used, these three sets of structures—the muscles, the bones, and the ligaments—will fix the thoracic cage in this position, and the possessor will never be able to expand his chest to a greater extent.

Further, the spine takes part in full and healthy respiratory movements, being extended in inspiration, flexed in expiration. Hence if full respiratory movements are not employed, the spine gradually becomes fixed in a more or less flexed position, the shoulders become round, and the scapulæ prominent. On the other hand, a man with good chest movements has an erect spine, square shoulders well held back, and a full chest. Still, let it be borne in mind that it is the mobility and not the mere external measurement of the chest which is of importance.

These remarks at once recall those who walk with good and those who walk with a bad carriage. The results of a bad physical education are obvious, while the outcome of deficient intellectual training is only manifest on closer acquaintance. Yet we have allowed the latter factor to dominate in culture, and to tend to make us all brain and little body, just the opposite to our early ancestors, who were all body with little mind. Both parts of our being must progress together or the result is unharmonious.

The preceding remarks refer to vigorous exercises in healthy or fairly healthy people. This course has been adopted because what rigorous exercises are to the strong, mild exercises are to the weak; and from a study of the former we can deduce the importance of the signs of distress in the latter. The chest should be the chief portion of the body to be steadily developed. Respiratory exercises should be taught, and respiration carefully attended to during gymnastic exercises. It may be desirable to allow the weak frequent intervals of rest, and perhaps to take a breath between each movement of the exercise. Also let it be remembered, *it is not the actual size of the chest, but the difference between the*

measurements of full expiration and full inspiration which gives the true idea of the capacity of the chest for expansion. It is this capacity for expansion which is the nearest available index of the athletic capacity, and except for accidents, of the individual's expectation of life.

The lessons to be learned by the instructor in physical exercises from these remarks are that chest exercises are the most important of all; good expansion being aimed at during the movements, and especially in weakly and delicate subjects, the respirations, the colour, and the pulse should be watched; and if there be any marked increase in the pulse rate (over five per minute) the lesson should be stopped or interrupted for a rest.

7. **The Nervous System and Exercises.**—The question under discussion is by no means simple, for it includes not only the influence of exercise on the nervous system, but also the influence of the nervous system on the performance of exercises.

(1) *The Influence of the Nervous System on Exercises.*—It is necessary to consider this, because the more feebly developed, weak, or run down an individual is, the more have we to count in practice upon the influence of the nervous system on the exercises. The peevishness of those in ill-health is proverbial. To make this point clearer, it will be advisable to give an instance from the life of an ordinary healthy person. Who has not undertaken a course of exercise with dumb-bells, and after a varying period discarded them? The habit has become a burden, or, in other words, the central nervous system has become wearied, and, as a result, the exercise has been abandoned. This occurs far more quickly if the nervous system is run down or enfeebled than in those who are physically fit. The story of the dumb-bells is only too often that of many exercises performed at home. And in practice it is impossible to lay too much stress upon the prime necessity of adjusting the exercises to the tone and inclination of the nervous system. It is well known that no exercise has much benefit for the person who has no keenness in its performance. These people often have for their only object getting the exercise over and done with. It is fully half the battle if the patients' minds can be interested in their exercises. This is often the greatest difficulty which an instructor of weakly children has to encounter and overcome. At the same time it is one of the great advantages of the so-called resistance exercises, that they are done against the muscular resistance of an intelligent instructor.

(2) *The Influence of Exercises on the Nervous System.*—In order to form an estimate of the value of physical exercises on the development of the brain, it is necessary to turn to the newly born. In a baby it is obvious that the neural and muscular mechanisms are to a certain extent fully trained, and ready to begin work at birth. Its heart has already been doing duty for some months; its respiratory muscles work well the moment it is born. But though it has limb muscles it can only use them imperfectly, aimlessly, and casually. As it grows up it is taught, either by itself or its nurse, to perform certain movements, and the muscles are thus educated

and brought under control. For instance, it is taught to speak and to write. These elementary facts illustrate the importance that the physical development of the body has on that of the brain. The education of the one is also the education of the other. But it is the body which educates the brain at first, rather than *vice versa*. It is a much later stage in development when the brain has become so educated that it can utilise its power and knowledge to teach the body. The relation between the motor areas and the intellectual centres is very interesting. Some great men have taken very little exercise, such as the late Professor Clerk Maxwell, the great physicist. On the other hand, very many men whose intellectual life has been long have been athletes when young, or have constantly taken exercise. As Professor Romanes pointed out, the word recreation, re-creation or making again, is very happy. Men of brain-work must constantly recreate themselves with active exercise. The motor areas of the brain have been likened to a battery which furnishes power or potential for the supply of the demands of the intellectual centres. And in this apt simile there is much truth; as we all know, exercise "clears the brain." A vigorous heart, efficient respiratory and digestive systems, are absolutely needful for the healthy activity of the brain.

It is unnecessary to emphasise further the intimate relations which exist between the health of the mind and that of the body. This relation is infinitely more delicate and liable to be upset in the weakly or convalescent than in the strong: an axiom which all interested in physical exercises must bear constantly in mind.

(3) *Exercises demanding Attention and Exercises not demanding Attention.*—By the phrase "not demanding attention" is really meant making very little demand on attention, and being, therefore, only accompanied by very little expenditure of energy on the part of the central nervous system. For every exercise demands some expenditure of nervous energy. In certain cases which need exercises the nervous system is so much run down and enfeebled that it is advisable to make only the smallest demands upon it. Consequently exercises which demand much continued or strained attention are not ordered. For instance, in recommending bicycle exercise, advice would be given that at first the pace should be easy, and the roads quiet, broad, and good. The rider can then get the muscular exercise with very little expenditure of nervous energy. Exercises done by imitation are less exhausting than those done smartly by word of command. The severe fatigue which ensues from the constant exercise of the attention is perhaps most strongly realised by the mountain-climber in the differences between the ease and comfort of running down snow-slopes and the severe tax of picking his way downward over a slope of scree or large stones, when every step entails care and attention. A more vivid illustration, perhaps, is the constant strain entailed in standing for a long time in steps cut in an ice-slope.

Exactly the same reasoning applies to the attention which must be given when the exercise is done by word of command. The constant

desire in instructors for a smart appearance during drill may easily lead to much damage to the nervous system of the members of the class. The more weakly may be unfit to sustain the loss of nervous energy required, and in consequence the exercises are done listlessly and without interest, and had better not have been done at all. This illustrates yet again the harm to individuals which may result from class-instruction, and it is difficult to insist too strongly on the necessity of having an inspector present to look to the individual units of the class and not to the exercises. A very decided test of the wisdom of stopping the performance is trembling of the limbs or outstretched hands. If this is present, it can be inferred that a good deal too much energy has been expended, and that a rest, if not cessation of the exercise, is necessary.

In dealing with the more healthy, difficulty may be experienced in deciding whether the nervous system or the heart is the source of trouble. For instance, the individual who shows a lack of staying power in a race. In the majority of cases I believe that it is the chest which is primarily at fault; a nervous system which is deficient in staying power is often associated with that condition.

8. **Exercises in the Period of Growth.**—The study of the influence of physical exercises upon the structures of the living body has revealed that every tissue in the body is affected profoundly: the bones directly through the pull of the muscles, the others indirectly through the nerves, blood-stream, and lymphatics. The age of childhood, and indeed that of the whole time of growth, deserves special study. This period, and especially the first half or two-thirds of it, is the only time in the whole course of life when the most far-reaching results may be obtained. During this epoch the tissues, by virtue of their power of growth, are as the clay in the potter's hand. Then can be obtained the finest result, or model, which the clay supplied is capable of. But it must be remembered that some clay makes fine china or porcelain, whilst other is only fit for the manufacture of the coarsest vessel. Still, without regard to the quality of the clay, childhood and early youth are *the* time when the surgeon, physician, or physical exercise instructor can obtain the best result of which the given child is capable. When this period has once gone by, comparatively very little can be done. And our object should be more to prevent mishaps which would diminish the physical or intellectual powers than to increase or perfect them. The machine is made, and we can only oil its joints and prevent the parts rusting from disuse. By education of the nervous system we can minimise the wear and tear of its daily work, the movements becoming automatic, and causing no expenditure of energy on the part of the central nervous system. In early life we must recognise that more can be done in the direction of removing the results of errors of development or deformities of mind, body, and health, than in bringing any additional influence to bear on the progress of disease. In children, unfortunately, there is often less chance of arresting the advance of definite morbid processes than in adults.

All growing matter must progress according to the dictates of two main influences. The primary one of these—the *growth by type*—determines that the fœtus of the human being becomes a man or a woman, and not an elephant or giraffe. The second is *growth according to function.* The word function is used in its widest sense, and includes both internal and external physiological influences, such as those of environment. Growing matter will react to these influences like a jelly set in a shape. This has been insisted on in connexion with the bones, inguinal and other regions of the body. Physical and intellectual exercises are able to mould the mind and body through their powers of growth. It is the growth, not the temporary moulding, which does the work. Growth is the active agent, the moulding is the passive. Hence the very slight value of the movements called "mouldings" in Swedish exercises. It is by active physiological use, and not by passive anatomical manipulation, that we can influence the body for good.

For many centuries children have received instruction for their minds; and as the pressure for intellectual attainments has become greater, the culture of the body has become inadequate, not having kept pace with the ordeals to which the young mind is now subjected. Of quite recent years it has become recognised that mentally deficient and backward children require special teaching, and it must also be recognised that a deficient body demands special cultivation. The cultivation of the body upon scientific principles should be studied in all schools just as surely as is that of the mind. Such exercises, judiciously chosen, will benefit all, from the young athlete to the newest weakly boy. Many fail intellectually in their after-life for the lack of cerebral development, or perhaps from the lack of cerebrum to develop. Let it be remembered that quite as many fail in physical life on account of deficient chest development. The instructor should pay special attention to this part of the body, and less to measurements round the limbs, such as round the biceps or calf. The larger the muscles are, the greater must be the amount of expansion of which the chest is capable.

Considerable tact must be used in the carrying out of the full plan of physical instruction, for it will be obvious that some members of the higher classes in intellectual work will rank very low in the scale of physical strength, and are in the greatest danger of having both minds and bodies seriously strained. But as in practice individual instruction on a large scale must be impossible, the evolution of a system in which as few as possible of the weak ones are damaged seems the best method obtainable. Classes for intellectual and for physical instruction can never be made up of the same pupils.

Boys under eighteen ought not to be subjected to exercises of the same degree of severity as men. Such sports as putting the weight or throwing the hammer should be done with lighter implements. Again, young boys should not be encouraged to spend too much time in the gymnasium. Premature development of the muscles of the trunk and limbs will lead to early union of the epiphyses and to stunting of the growth.

The sport that will enable boys to attain the fullest development of which they are capable must give play to all parts; quick movements of the body, rapid decisions of the mind, skilfulness of each player among his fellows.

II. Physical Exercises

1. Degrees and Principles of the Methods of Physical Exercise.—Massage in its various forms may be regarded as stages in the "positive degree" of exercise. Physical exercise, adapted for the improvement of those convalescent or by nature delicate, may be regarded as the "comparative degree"; whilst the sports and pastimes, by means of which the naturally strong improve their condition, represent the "superlative" degree. Exercises of the "comparative" will be described here, whilst those of the "superlative" will be mentioned in order to illustrate certain points.

The muscles are by far the largest storehouses and manufactories of energy in the body. By exercise or rest the output can be varied; and by these means all the other tissues of the body can be influenced more than is possible in any other way. It has been usual to subdivide physical exercises into preventive, medical, and educational, or into therapeutic and hygienic gymnastics. Such classifications are cumbersome. The science of the art of exercise lies in adapting the methods to the material to be worked with. Classifications do not aid much in this; besides, they introduce the idea of classes and divisions containing many units, whilst the best results of physical exercise are obtained by individual attention. In the "positive degree," massage, the attention is given wholly to the individual; so must it be for exercises of the "comparative degree," that is to say, when it is given to the weak. In the further degree, exercise in the strong and healthy, such special care is not required. Exception must always be made of those within the period of growth, say up to the age of eighteen, to whom more care should be given than at any other time of life. During this period our object is to fit the individual for a vigorous, strenuous life of use to the community; whilst later we can only rehabilitate a decadent or diseased body. In general, and from the sociological point of view, the former is by far the more important, though perhaps not so much from the ethical standpoint.

Before entering upon the subject of the exercises, a few points must be mentioned to account for the formulation of certain generally accepted and advocated rules.

With regard to *fatigue*, we must recognise that it is at least of two-fold origin, nervous and muscular. Mental fatigue is a factor to be watched for, particularly in the young, the weakly, or the invalid. Thus, for indolent-minded people or those sedentary in body, it will be best to order a graduated series of exercises which require some orderly effort of mind and will in the execution. They can be taught the more complicated exercises; or, if they are well enough, riding, rowing,

and other games. But in people whose nervous system is run down (neurasthenics), a precisely opposite course must be advised, such as will not demand the least nervous effort. For the former, active movements are most suitable; for the latter, passive movements, especially those of the subdivision known as massage. Six general rules may now be quoted:—

(1) In the weak care must be taken to avoid degrees of fatigue, which do not pass off after a few minutes' rest. At first movements must be slow, and should always be preceded and succeeded by light massage. As strength is gained the movements are to be continued longer, and pushed until a greater degree of fatigue is experienced.

(2) When commencing treatment with exercises, pay special attention that the respirations are properly performed, stopping every now and then to allow a number of quiet breaths to be taken. Avoid causing breathlessness and palpitation.

(3) Exercises should be repeated daily, about the same hour, and should cease so as to allow a rest of half an hour before a meal. They should not be given just after a meal.

(4) In correcting special infirmities see that the movements are done very slowly, especially at first. Later, or for the improvement of the general condition, rapidity is desirable.

(5) Exercises are most beneficial when carried out, as after bathing, stripped and in the open air. But for ordinary purposes it is only necessary to see that the room is bright and airy, and that no clothes are worn which in any way interfere with perfect freedom of movement or the action of the skin.

(6) It is advisable before starting exercises that a medical man should report upon the conditions of the heart, lungs, and abdomen, and that certain data be noted, viz. the amount of expansion of which the chest is capable, as measured by the difference in the circumferences of the fully expanded and contracted chest, and the height, the weight, and girth of the abdomen. Other measurements can be taken, such as those of the limbs. This examination should be repeated at regular intervals of a fortnight or a month by the same medical man, who can then note the improvements and alter the exercises as may be indicated.

In this last rule the question is raised as to the relations between the medical man and the instructor. Or, as it may be put, the relations between the science and the art of physical exercises. Of course the ideal condition is to have the offices combined in one individual. But practically there are very few medical men who can give as much time as is necessary, except perhaps in very special cases. It is better that an instructor should carry out the art, whilst the science can be directed by the medical man. A great deal of the charlatanism which surrounds the subject has arisen from the fact that the instructors, by means of the acquirement of a few anatomical and scientific terms, have converted themselves into "professors."

Exercises may be performed in at least two ways: the movements may be slow or rapid. The slow movements are best for the feebly developed, the convalescent, and the prematurely aged. The muscles are thus strengthened, and in the slowness of the movements there is very little expenditure of nervous energy. Rapid movements are obviously unsuited to these persons. They have less effect on the muscles than on the nervous system. For their performance they presuppose good muscle, and are largely useful in improving the condition or the training of the nervous system. The reason for commencing training with slow exercises is to improve the muscles. Quicker exercises follow, until finally both muscles and nervous system are braced up.

2. The Movements and Systems of Physical Exercise.—The various movements employed in the exercises of the comparative degree, *i.e.* for the weakly and the invalid, may be defined as follows :—

An active movement is one which the patient himself makes by the expenditure of his own strength. All the movements in exercises of the superlative or third degree come under this heading.

A passive movement is one which is performed without the patient using any force at all. Every movement of the positive or first degree comes under this denomination. The whole of massage consists of a series of passive movements, which, however, need not concern the muscles directly. These movements are of little value in exercise, and are only to be used in very weakly subjects who have been in bed for a long time, or in the treatment of joints.

A movement of resistance is one in which the movement may be carried out or resisted by the instructor or the patient. The movements are of much more therapeutic value than the merely passive ones, and form a transition from them to the active. They are further employed, as in the superlative or third degree, for improving the general condition. In this case they are usually made against a mechanical and impassive resistance, such as dumb-bells, pulling and lifting weights, etc. Other apparatus are less impassive, being made of rubber and having a recoil. As examples Whiteley's exerciser and the pugilist's punching-ball may be mentioned. All active and resistance movements require some expenditure of nervous energy, and are apt to pall and become a burden, especially to those in an enfeebled state of health and strength. This weariness can often be obviated by means of rests and judicious variations in the exercises. Another kind of resistance movement is practised against human, and therefore adaptable and active, resistance. This is the great advance which the Swedish exercises have made. They are much more interesting for the patient, and can be adapted to limit the outflow of his nervous energy. Such personal exercises possess great advantages over the mechanical contrivances.

This is a suitable opportunity to refer to the various systems of exercise. Although there are a number of these, there are a far greater number of exercises invented. In fact, every teacher creates a system of exercises according to his or her quantitative possession of common sense.

The Swedish system was invented by Ling, whose name is sometimes given to it. When Ling died in 1839, two institutions had already been started in Stockholm, namely, in 1813 and 1827 respectively. Dr. John K. Mitchell (6) says: "General medicine owes much to Ling's propaganda in the spread of information about medical gymnastics, though not so much as the Swedish authors would have us believe. Valuable as Ling's work was, the school founded by him has degenerated into a kind of barren formalism; the system has become a sort of religion in which faith replaces knowledge." These criticisms are true for the more ignorant of those who work in the name of the Swedish system, which should be judged by the smaller number of excellent workers who do honour to their *alma mater*. Unfortunately it is hampered by a clumsy terminology, in which, however, the various movements are so named that it is possible to prescribe exactly the movements to be used. For instance, "Stretch leg-forward-lying double plane arm-carrying," or "Hips-firm high stride-sitting trunk-rolling,"—terms which may be useful to those who have been trained in the system, but which effectually prevent its popularity.

The exercises are built up upon four fundamental positions, the standing, sitting, lying, and hanging. The fifth fundamental position of kneeling has fallen into disuse. From these there are a number of derived positions and movements, for which the reader is referred to Wide's handbook. Suffice it to say, that the number of these derived movements is almost infinite. The practice of the exercises is progressive. The start is simple, these exercises being mastered before others are tried. But no matter how far a lesson proceeds, it is always finished off gradually, ending with slow exercises.

The Swedish system has become the basis of almost all the innumerable methods and exercises which do not demand the use of special apparatus or instruments. Of the latter only two will be mentioned, namely, Sargent's and Zander's.

Sargent's System.—Dr. Sargent, of Harvard, invented an incomplete system, intended to strengthen various groups of muscles by means of apparatus. The method is largely one of weight-lifting with machines; for example, he invented a kind of rowing machine with a sliding seat.

Zander's System.—In 1897 Dr. Zander invented two kinds of machines, one for massage, the other for passive and resistance movements. A very large number of similar machines have been invented from time to time by other people. The motive power is supplied by steam or electricity. These machines unintelligently perform the part of the instructor in the Swedish system.

The Japanese System.—Jiu-jitsu is one of the best and oldest in the world. It forms part of the general education, and a full course occupies four years. It includes at least six sub-systems, and aims at cultivating the physical, physiological, mental, and social capacities. The foundation of physical culture is laid in a sound digestion, and attention is then

directed to improving the working values of the heart and lungs, and then of the limbs and body as a whole.

One other instrument deserves special mention, the electric percussor introduced by the late Dr. Mortimer Granville. This percussor, or percutor, strikes about 1500 blows a minute.

Except with regard to the use of vibratory exercises machines are at a great disadvantage as compared with the help of a good instructor. Quick vibratory movements are of considerable use in some cases.

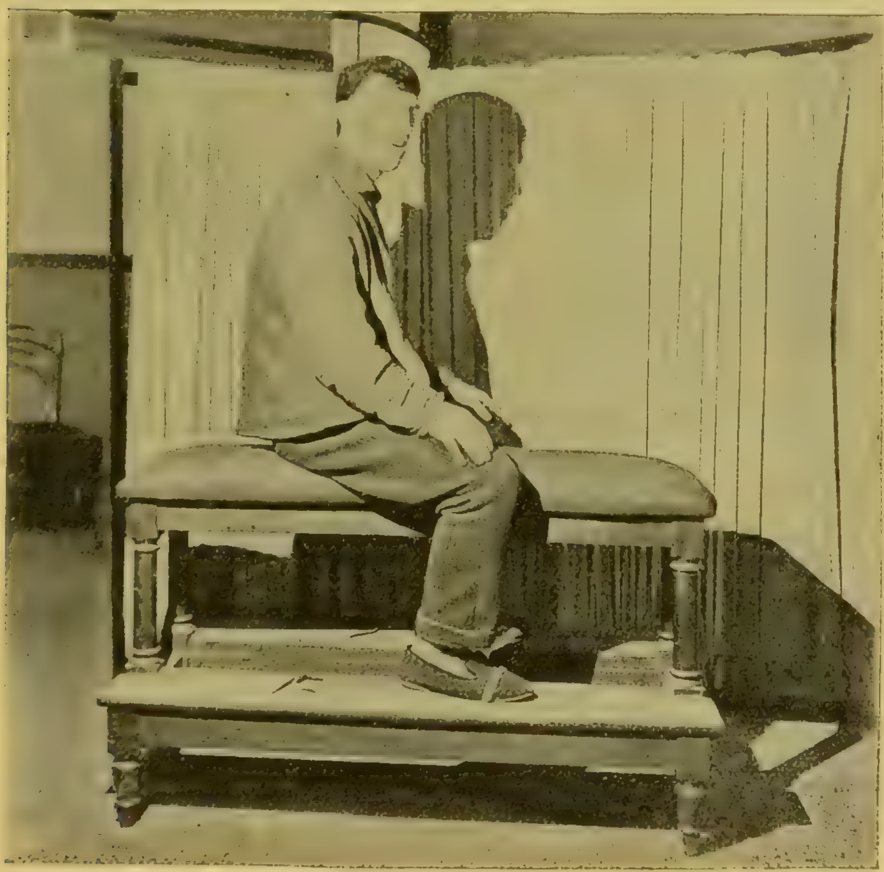

FIG. 2.—High plinth.

3. Apparatus.—The other apparatus can be roughly divided into two classes: those used for class and those for individual instruction. The former includes dumb-bells and barbells; the latter various apparatus, which will be briefly described. The best of all instruments for use in physical exercise is the resistance offered by the muscle of an intelligent instructor. In fact, the fewer instruments or implements used the better.

Dumb-bells should only be used as variations to exercises without them. They should always be light, for it is their presence, rather

than the slight passive resistance offered, for which they are employed. Barbells have one great advantage over dumb-bells in employing new movements and exercises, so making the variation from the routine more marked. They are also particularly useful in aiding respiratory exercises for chest expansion. Indian clubs are of very little use in physical exercises. The movements are rapid, and in consequence involve more expenditure of nervous than muscular energy,

FIG. 3.—Low plinth.

but the exercises are extremely varied and, consequently, interesting. They do, moreover, what no other exercises do, promote flexibility of the wrist. Instruments chiefly used for muscle-making, such as Sandow's squeezer, will not be described. The acquisition of huge muscles does not fit a man for life, but rather hampers him, unless his vocation is that of a bargee or a stevedore. The amount of "combustion material" formed by the contraction of huge muscles unfits a man for active, prolonged effort, such as running. In fact, such a soldier would be as incapable of charging as of running away.

Apparatus for Personal Instruction.—The best apparatus that can be used are the muscles of the instructor. No other apparatus is really necessary, but individual instruction can be aided with it. There are two forms of apparatus which are useful, and are called the high and the low plinth respectively. The high plinth (Fig. 2) is a seat about 40 cm. wide, and raised about 75 cm. off the ground. There is also a footboard on each side which is about 30 cm. off the ground. Attached to it are straps for fixing the feet or, when the patient is seated astride, the thighs. It is most useful for exercises of the chest and trunk muscles in the stronger patients. The low plinth, as its name implies, is similar but lower, being only about 45 cm. high (Fig. 3). But it differs in possessing an adjustable back and foot pieces; sometimes arm-rests are added to it. It is useful for weaker patients and for passive respiratory exercises. An apparatus called a peg-post is useful, but not necessary. It consists of a post fixed against the wall, on each side of which is a row of pegs made so as to be grasped by the hand, the pegs being about 12 cm. apart. Stools, made perfectly plain and about 40 cm. high, with the tops about 40 cm. square, are always useful. Other apparatus, such as Sargent's rowing machine with a sliding seat, are cumbersome, and are not sufficiently useful or needful to counterbalance this objection. A Whiteley's exerciser is useful, but patients should be shown how to work it properly, so that they may be able to correct their various deficiencies at home.

4. **Respiratory Exercises.**—As the various exercises of the limbs are easily learned, the only description given here will be of respiratory or chest exercises. Though it is little known, respiratory exercises can do a great deal for patients who are convalescent from pneumonia or pleurisy. Pleural adhesions can be made to disappear just as passive movements of joints remove synovial adhesions. Respiratory exercises educate the heart and keep it in good working condition. They are of great value in improving the tone of all the various systems in the body.

As in all other exercises, the first thing to insist upon is the need of doing the movements from the correct position. The assumption and maintenance of the correct position is in itself an exercise; and if the subject fail to maintain this, he is obviously unfit for harder work. The elimination of physically unfit units should be one of the first duties of an inspector of classes. This is most important in standing exercises. When standing in a bad position the muscles of the back and abdomen do not perform their proper amount of work, respiration is less deep and efficient, fatigue comes on early, and the therapeutic value of the exercise performed is lost (Fig. 4). In standing erect, the most frequent fault is to let the shoulders droop, when the chest flattens and the ribs are depressed, assuming *the attitude of rest.* Full, deep breaths are impossible in this position. With flattening of the chest the lower part of the abdomen is frequently protruded. This fault is corrected by bringing the shoulders back and expanding the chest, the *attitude of activity* being assumed. Another fault in standing

erect is that the shoulders are thrown back and the abdomen protruded as in a corpulent man or a pregnant woman. The position is accompanied by lordosis of the spine and sometimes by pain in the lumbar region,

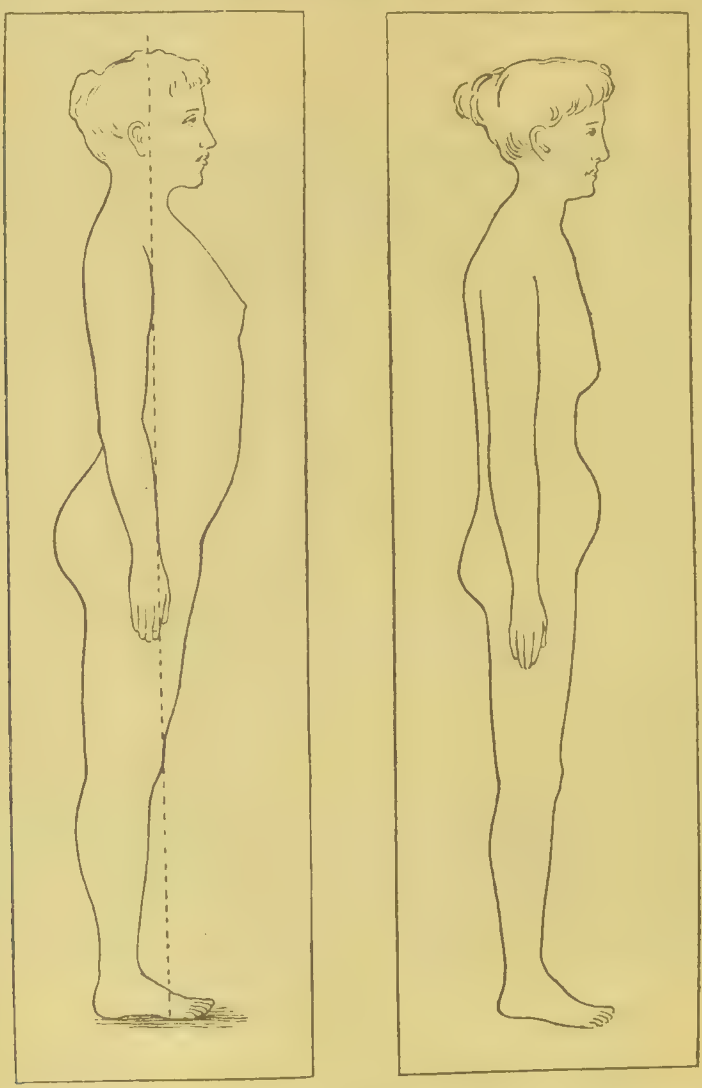

Fig. 4.

Figure of a healthy German peasant woman showing the erect attitude and the position of the trunk in activity.

Figure of a feeble American showing the slouching attitude and the position of the trunk in rest.

which will disappear with the cure of the fault. No one walks well who does not stand well; an easy carriage with a light step is the first and final expression of grace and strength.

General Breathing Exercises.—Natural breathing is performed by a

combination of thoracic and abdominal movements. The inspiratory movements of the thorax, namely, the elevation of the sternum and ribs, and the descent of the diaphragm, increase the capacity of the chest. Apart from the ordinary muscles which do this there are extraordinary muscles, such as those of the upper extremity. Thus raising the arms assists the inspiratory movements of the chest greatly. The abdominal movement consists of the excursions of the diaphragm, which may be aided by relaxation or contraction of the abdominal muscles. The thoracic type of breathing predominates in women, the abdominal in men. The chest movements can be increased by constricting the waist and abdomen, as is done by women's clothes and stays, but thoracic breathing is the type of respiration which is seen in savage women who have never worn corsets or skirts. The explanation of the method of breathing peculiar to women must therefore be sought in other factors, such as their adaptation for child-bearing, though doubtless some women impair the healthy disposition and the natural efficiency of their thoracic and abdominal organs by tight-lacing.

After a feeble patient has been taught simple leg and arm movements, followed by instruction in positions and poise of the trunk, it is best to begin at once with respiratory exercises in order to prepare the chest, enabling its movements to assist the heart in the severer trials, and at the same time correcting any faults. In this way the patient is fitted for further exercises.

Active Respiratory Exercises.—One action forms the true basis of all respiratory movements, and upon this foundation many and various exercises have been built up. This is the employment of slow, deep inspirations, which expand the chest to its fullest. When the chest is full the patient holds his breath for a time, about ten seconds, in order to raise the temperature of the inspired air, which will expand and further distend the alveoli of the lungs. These deep inspirations can be performed with the hands on the hips. Care should be taken that expiration also is fully performed, as it is the extent of expansive movements of the chest which is desired—not mere large external measurement. The force of the exercise may be increased if during inspiration the extended arms are slowly raised above the head and lowered during expiration. By raising the arms from the sides until they are in line with the shoulders, the chest is mainly increased by lateral expansion. If, however, the extended arms are directed forward and raised in this way the antero-posterior diameter of the chest is increased most.

Two modifications may be mentioned to both these exercises of raising the arms laterally or directly to the front during inspiration, and lowering them during expiration. Instead of merely pausing for a period of ten seconds, the knees are slowly bent and the trunk lowered and raised to the fullest extent; or, the trunk may be bent forward till the fingers touch the floor, and raised again. Then the arms are lowered and the air expired slowly.

These exercises may be done sitting or standing, preferably standing.

As an example of a sitting exercise the following may be mentioned: with the knees separated, the trunk upright and extended, expire whilst bending the trunk forward as low as is possible, clasp the hands over the back of the neck, then inspire, and raise the trunk to the erect position. This exercise is of more practical value in middle-aged than in young people.

All these exercises influence the thoracic more than abdominal respiration, and as this type of breathing is deficient in men, these movements are more adapted to supply their wants. The above have been mentioned as examples, and may be briefly summed up as follows:—

(1) Stand erect with hands on hips, inspire and expire slowly, allowing a pause of ten seconds or so between these acts.

(2) Stand erect and slowly raise the extended arms from the sides in a lateral condition, inspire during this; pause as above; expire and lower arms slowly.

(3) Same as 2, except that instead of raising the arms laterally they are directed forward and not brought quite over the head.

The intervals between inspiration and expiration in 2 and 3 may be utilised with advantage as follows:—

(*a*) The knees are bent and separated, the trunk lowered as far as possible, and then raised.

(*b*) The trunk is flexed at the hips until the fingers touch the ground, and then raised, the knees being kept straight.

(*c*) The body may be slowly raised on the toes, and lowered two or three times.

These movements may all be repeated a certain number of times, five, ten, or twenty, and carried out as slowly as is possible.

The breathing exercise in the sitting posture, which in the main consists of raising and lowering the trunk between the knees during inspiration and expiration, is a useful variation.

Passive Respiratory Exercises.—Respiration is performed naturally by means of an unconscious neuro-muscular mechanism. For it to take place at all, there must be some active muscular contraction, exception being made to the pure mechanical methods adopted for artificial respiration, such as are used in the resuscitation of the partially drowned. By means of artificial respiration we have become thoroughly aware that if an operator or instructor performs certain passive movements with the patient's arms, air is drawn into the chest. This process is used in respiratory exercises to increase the depth of inspiration. As in this case the subject is conscious and breathing, the method is used to assist and accentuate these natural respiratory movements. In practice it is best performed in this way. The patient sits astride the high plinth (Fig. 2). He is then instructed to breathe slowly. During inspiration the instructor, who is standing behind, draws the patient's arms upwards, pulling on them when they have reached their full extension. By this procedure an extra quantity of air is drawn into the chest mechanically, and, as it involves little or no expenditure of

nervous energy by the patient, it can be used when active respiratory exercises cannot be tolerated, or are badly performed. By using only one arm, or by pulling more strongly on one when using both, the corresponding side of the chest is more forcibly expanded. In unilateral lesions, or deformities of the chest, it is very useful to employ this modification of passive respiratory movements. It could be employed in the relief of adhesions due to unilateral pleurisy. It will be referred to in the short account given of the treatment of cases of scoliosis (p. 418).

For the benefit and improvement of abdominal breathing far less can be done; the diaphragm is always the best conditioned muscle in the body, and is, in consequence, susceptible of but little improvement. A deep inspiration is taken, the abdomen protruded, and the body bent backwards. At the same time the arms, which have been at the sides, are carried a little backwards with the palms directed forwards and outwards. From this position the extended arms are slowly raised to the vertical and then carried forward till they are horizontal. During this movement a thoracic inspiration is added to the previous abdominal one. After a short pause the air is expired, and the arms allowed to fall to the sides.

The practice of bandaging the upper part of the chest or the abdomen, according to which type of breathing is to be developed, is abominable. These respiratory exercises should be carried out before the bones and ligaments of the spine and ribs become "set" by maturity and the cessation of growth.

The exercises described have served for the voluntary or conscious development of the respiratory movements. For the involuntary or unconscious teaching of the same lesson, it is found that the results are better the larger the amount of muscle employed. Thus leg exercises are better than arm. Best of all is steady running at a middle speed. Walking up-hill is also very good. For stronger people short, sharp sprints, with easy walking in between, will do most.

Uses of Respiratory Exercises.—First of all, exercises must never be given when acute disease is present. The old, those with marked disease of the heart, arterial system, or lungs, must have slow, steady movements carefully administered. Young, fat, and idle people should have quickly increasing exercises which demand activity both of mind and body. For instance, an hour of fast walking is said to be equal to a quarter of an hour of slow, steady running. All exercises, especially if large groups of muscles are used, improve the chest and respiration. But it is often advantageous to employ in addition special respiratory movements, or the latter may be used to relieve some defect. The special value of respiratory exercises may now be discussed. Briefly, they may be used as an aid to normal or to backward development, as an aid to convalescence, for deformations of the thorax, for some diseases of the viscera therein contained, and for general purposes.

(1) They are of prime importance in cases of feeble but normal development. For this purpose they should be employed during child-

hood and early adult life, say between seven and seventeen years of age. In cases of rapidly growing or over-grown children, the chest development is always the chief deficiency, being usually sacrificed for that of the mind and limbs.

(2) If these exercises are used later in life, they are of value in reinvigorating the whole system, by improving the heart's action, and in "sweeping the various chimneys of the body."

(3) *Deformities of the chest*, such as involve the ribs and sternum, and commonly result from rickets, can, to a very large extent, be rectified by exercises during childhood. The subject of the condition is given fuller expansion of the lungs, and saved from much disability and disposition to disease.

(4) *Spinal deformations*, such as occur in the rickety and feeble, should be carefully treated in this way during childhood and youth. The gross curvatures of scoliosis, kyphosis, and lordosis will be briefly considered later. Young children and adults frequently lapse into slouching habits —not standing erect, but leaning forward; to this position the growing spine adapts itself. Respiratory exercises will give an erect, alert carriage in which the normal movements of inspiration are accompanied by extension, and expiration by flexion of the spine, the mobility of which is thereby retained.

(5) Exercises are useful in *diseases of the heart*, but only a brief mention will be made of Schott's and Oertel's methods of treatment.

(*a*) In the healthy, exercises are of great value in improving the muscular tone of the walls of the heart, and during preparation for the more violent exercises, such as rowing, in teaching the nervous system to co-ordinate the work of the heart and lungs, and fitting these viscera for the severest test.

(*b*) Some affections of the myocardium, degenerative changes, and fatty infiltration.

(*c*) Some affections of the pericardium following pericarditis, and for adherent pericardium. The exercises must be carefully carried out under the supervision of a physician.

(6) Some *affections of the lungs*: for instance, very early tuberculous disease with deficient expansion of one apex. Exercises should be used as a preventive measure for the latter condition. After pneumonia and broncho-pneumonia exercises are most useful in assisting to remove traces of consolidation and collapse. Almost any disease which affects a lung will leave behind a condition which is capable of relief by physical exercises.

Emphysema and chronic bronchitis are distinctly diseases of adult life, and therefore occur at a time when the thoracic movements are limited. Exercises cannot possibly bring much relief to these patients, whose chests are more or less fixed in a position of inspiration. Still many cases have been improved by forced breathing. Some forms of asthma have been relieved and even cured by courses of respiratory exercises.

In *pulmonary tuberculosis* exercises may be given carefully, and are frequently beneficial. They must be employed only for short periods several times a day. The breath must only be held for a very short period. According to its pathology, physical exercises should only increase *bronchiectasis.* In young subjects the increased power of expansion of the chest would assist in forcibly evacuating the contents of the cavity, and lead to both general and local improvement.

After *pleurisy* a number of adhesions are formed, and convalescent cases should therefore always be submitted to a course of respiratory exercises. As yet there is no knowledge of any ill effect in cases in which the pleurisy is of tuberculous origin. When an *empyema* has been opened the lung collapses. The rate of the subsequent expansion of this lung has a great influence upon the course and duration of the convalescence. As soon as the acute symptoms have subsided it is advisable to begin a graduated series of exercises. Vigorous inspiratory movements will be most beneficial.

Constricting bands round portions of the chest or abdomen have been used for the expansion or removal of adhesions from portions of the lungs. For instance, for the expansion and removal of adhesions from the apex of the lungs the lower ribs have been firmly strapped before the exercises are undertaken. Such a constriction throws the more work on the freer parts, and is said to act beneficially.

(7) By respiratory exercises the aeration and circulation of the blood is much improved. As a result all the vital processes of the body are quickened, and the work is done with renewed energy. The important function of digestion is stimulated, while the activities of the great excretory organs, the kidneys and the skin, are increased. Thus it is easy to conceive how it is that under such treatment a man's eye brightens, his mind becomes more active, the glow of health returns to his cheek, his appetite increases, sleep becomes more refreshing, and his step, instead of languid, becomes quick, steady, smooth, and elastic.

(8) Reference still remains to be made to the *abdominal effects* of respiratory exercises. Apart from the general improvements mentioned above, a tendency to sluggish and inactive bowels is relieved, the abdominal muscles become strengthened, and in some women the pains of menstruation are relieved or abolished by a course of exercises.

In considering diseases of the pleura and pericardium the efficacy of exercises in removing adhesions was mentioned; the same beneficial effect is produced in the abdomen by the increased excursions of the diaphragm. The removal of adhesions explains the relief or cure of some cases of dysmenorrhœa, while similarly the disappearance of adhesions in other situations may lead to the cure of obscure abdominal pains. After operations for such conditions as localised abscesses or general peritonitis, in fact, after most abdominal operations, a course of exercises will add not inconsiderably to the measure of success attained. The strengthening of the abdominal muscles will tend to prevent hernial protrusions both in the ordinary positions and in the scars of operations.

To sum up, respiratory exercises, apart from their special effects, improve the action and condition of all the glands in the abdomen: and further, as a result of the improved conditions of the vascular and

Fig. 5.—Figure of a boy with nasal obstruction due to adenoids. The chest is flat, the shoulders rounded, scapulæ wing-like, and the abdomen protruded.

digestive functions, the tone of the whole body, from the nervous system to the nails, will be raised.

Nasal and Oral Respiration; *Adenoids.*—If one watches instructors at work, or reads the instructions as to the way in which exercises—and

especially respiratory exercises—should be carried out, one is struck by the want of care and attention paid to the point whether the breathing is carried out through the mouth or through the nose. Even medical men pay very little attention to the manner in which respiration is performed, yet it is extremely important for the well-being of adults, and far more so in children, to see that nasal respiration is efficiently carried out and performed. As a result of mouth-breathing, the nasal cavities are insufficiently aerated and cleared, and in consequence there is an infective condition of the mucous membrane of the nose; and later, hypertrophy of the lymphoid tissue of the naso-pharynx or adenoids. The obstruction caused by these still further militates against the acquisition of the habit of nose-breathing. Mr. Arbuthnot Lane (15) has urged consistently for the last ten years, that the full development of the upper maxillæ depends upon the proper habit of nasal respiration being acquired during the period of life when these bones are susceptible to change, that is to say, during childhood. To quote his words, "the whole of the cavity of the naso-pharynx is increased in size, the palate descends, the alveolar arches of the upper and lower jaws increase in breadth, and the malar bones become more prominent owing to the greater development of the central cavity in the superior maxilla" if nasal respiration is properly established. This result of proper nose-breathing explains the occurrence, so frequently seen in adults, of thin noses, flat cheeks, and high palates; especially in women on account of their lack of proper exercises. A burden is added to that which parents, and perhaps schoolmasters, already bear, and their failure, should it occur, is written boldly across the faces of their children. No more is needed to impress all instructors with the prime importance of seeing that children breathe well and easily through their noses. With regard to those above eighteen or so, the damage to the shape of their noses, cheeks, and palates is irretrievably done. Further, it is not so easy to instruct and accustom them in nasal breathing, which it is not infrequently impossible to render adequate to their needs. In children this is not so; persistent teaching will almost invariably be crowned with success, the ever-widening growth of the nasal cavities helping. The flat chest, deficient in expansion, which accompanies bad adenoids, is seen in the illustration.

The operation for the removal of adenoids is unsatisfactory or worse in a large percentage of cases, if nasal respiratory exercises are not taught afterwards. These may be started a few days after the operation, when any inflammatory swelling has subsided. It is always advisable to impress upon parents that the subsequent respiratory exercises are quite as important as the operation itself (*vide* article on "Adenoids," vol. iv.).

III. Treatment

Before discussing the various diseases and conditions amenable to treatment with exercises, it is advisable to indicate those in which harm would result from such practice. Much charlatanry exists in the

pretensions to cure acute diseases by massage and exercises. For, as a matter of fact, all acute diseases are beyond the scope of exercise, and ought to be treated by rest. Yet cures of acute prostatitis and of other affections are reported by the ignorant. Diseases of infective origin, such as tuberculosis, syphilis, those due to pyogenetic and other organisms, cannot be directly benefited by exercise ; and though the patient may be indirectly improved in subacute cases, in the more acute he will be directly harmed.

It must be clearly understood that exercises can correct weakness, deformity, and perhaps deficiency ; but they cannot cure disease. In the majority of cases the most that can possibly be done is to relieve symptoms. For such purposes exercises are employed in heart and nervous diseases.

1. **General Obesity.**—The use of physical exercises is the only part of the treatment of obesity that will be considered here. Fat people may be divided roughly into two classes—the healthy and the unhealthy. The healthy ones, who are chiefly young, should be ordered gradual and increasingly severe exercises, demanding ample expenditure of nervous and muscular energy. All the exercises must be pushed to the point of moderate fatigue. Fat people are, however, usually in the period of middle age, when it is not desirable to prescribe violent exercises. The two most important symptoms of distress from which such persons suffer are shortness of breath and palpitation. These naturally interfere greatly with the exercises and militate against the successful removal of the fat. Respiratory exercises will do much to relieve them, as will also strict attention to diet. If obese people take more exercise than is good for them their temperature rises, the fatigue fever as it is called. The pyrexia is transient and apparently due to the fact that, being ensheathed in a layer of non-conducting fat, they cannot get rid of the heat formed by the contraction of their muscles. Exercises must be begun moderately in such subjects, and slowly increased. When they are ready for it, skipping is one of the best exercises which they can take at home.

Attention should be directed to the abdominal muscles which are in poor condition, and, owing to the deposits of fat in the omentum and elsewhere in the abdomen, are stretched and distended. Abdominal massage, abdominal respiratory exercises, raising the trunk or legs when lying on the back, or raising the knees as high as possible when standing, are most beneficial exercises in lessening the girth measurements. It is, however, impossible to detail all the various exercises which have been employed for the relief of obesity. As in other conditions, the actual exercises employed largely depend upon the application of ingenuity and common sense to the ends required. All through, but especially at the beginning, watch must be kept for palpitations and breathlessness, and it is advisable to have the patient regularly overhauled by a physician at definite intervals of one or three months.

In cases of ordinary obesity much relief results, and will last so long as the patient does not relapse into his former ways. In other cases only

temporary relief can be obtained. And in the most difficult cases of all it is found that the loss of nervous energy, consequent upon the exercises given for the removal of the fat, is too great. The patients go from bad to worse, and eventually drift into the condition of Adiposis dolorosa.

2. **Heart Diseases.**—Physical exercises are not used to cure disease of the valves, but to improve the working capacity of the heart muscle. There are two chief systems of treatment—Schott's and Oertel's—in which physical exercises play a part. With the other portions of these systems we have no concern here. When by means of rest and treatment compensation has been restored, it is the duty of the instructor in physical exercises to begin the education of the heart muscle, and thus improve its efficiency. For obvious reasons this has to be done very gently and slowly, and the treatment may extend over months or a year. At the outset, slow passive movements of the limbs are used, such as simple flexions and extensions, the patient lying down. From these advance is made to gentle but increasing resistance movements, until the patient is well enough for the exercises to be taken in the sitting or standing positions. Passive and, later, active respiratory exercises may next be added. Walking uphill is begun gradually, increase in the amount done constituting the keynote of the treatment. Great care must be taken to avoid palpitation, breathlessness, quickness or irregularity of the pulse. But exercises form only part of these methods of treatment, though they are the important educational part. For further details reference must be made to other sections on diseases of the heart. For special selection of cases for treatment by exercises, those with moderate or failing compensation, particularly when connected with mitral incompetence, cases with functional palpitation and tachycardia, those with fatty hearts, general stoutness, and shortness of breath may be mentioned. In others, until compensation is established by rest, physical exercise plays no part in the treatment.

3. **Nervous Diseases.**—Exercises are sometimes employed for the relief of certain symptoms of nervous disease. They are of use in two ways: first, by keeping the muscles in good condition; and, secondly, the constant repetition of simple movements re-educates the nervous system as regards co-ordination. They have been most used in locomotor ataxy in order to relieve the ataxia. The process of teaching is a very slow one, as the patient has lost sensation in his muscles and joints. Special care must be taken to avoid fatigue, as the patient has lost his sense of it also. The exercises must be taken first in the recumbent position, be simple, carried out slowly, and often repeated throughout the day. The lessons must be short at first. When these simple movements have been learned, they are to be repeated with the eyes shut. Massage is a useful accompaniment, but it must be done gently. Next, simple exercises are taught in the erect position, first with eyes open and then with eyes shut. The movements must be slow and steady. Walking steps must be taught, letting the various movements be done slowly and in an exaggerated fashion, the leg being raised higher than

necessary. Walking along a line, between obstacles, over steps, or at a mark, are more complex exercises, and can only be done when the patient has recovered his loss of power of co-ordination to a considerable extent. Sitting and rising movements will aid to complete this second education. Throughout great care must be taken to avoid the evils of over-exertion and fatigue, since as the patient's feelings are of little or no use on this point, they are very likely to be overlooked. A mistake in this respect will very likely destroy all the good which may have been done towards regaining power of co-ordination. The prognosis is not good. The results of treating these cases are frequently disappointing in practice, and the apparent benefits slight. On the other hand, in some cases the improvement is remarkable, not to say brilliant. For instance, a tailor recovered so much as to be able to do his work for years. The result depends on two factors, of which the most important is the extent and stage of the disease, and the other is the natural aptitude or ineptitude of the patient to learn. It is impossible to say what results will occur until the experiment is tried. Some authors have advocated the use of exercises in all early cases, believing that the onset of the ataxy is indefinitely postponed thereby.

Exercises have been urged in any nervous disease associated with ataxy. In paralytic lesions it is only of use in preserving the muscles until surgery, by nerve suture or grafting, comes to their aid. This is not often the case, but the brilliancy of one successful result overshadows many failures. In paralysis of the facial nerve, in connexion with middle ear disease and operation, it is most important to keep the facial muscles in good condition by massage, exercise, and the battery until successful nerve union has followed suture. If the measures for the preservation of the muscles are neglected, fibrous tissue will have replaced the muscular fibres, and the neuroraphy will be a failure. A similar argument might be applied to the results of anterior poliomyelitis. Surgery is, unfortunately, of little use to the unfortunate sufferers from this disease. Some of the initial paralysis clears up. Massage and movements are very useful until it is known exactly which muscles are affected and which have escaped. Similarly, movements are useful in the various forms of neuritis, such as that due to alcohol. Sciatica may be much improved when once the acute symptoms are over. Physical exercises are of great value in treating debilitated people and those suffering from neuroses, but must be employed in the later stages of treatment. Whether the debility has arisen from objective causes such as drug-habits, or from purely subjective reasons, as in the neurotic, does not matter. Exercise restores tone to the various systems of the body, and much of the future success of the "cure" depends upon the patient acquiring an interest in some form of exercise in the open air.

To the lack of this may be attributed many of the failures in those who have been "cured" of the morphia habit. At first, care must be taken not to use exercises which cause any great expenditure of nervous energy. The nervous systems of debilitated persons are already run

down. When rest has already done much to restore them, exercises are called in, not to expend the whole of their little supply of nervous capital, but to increase it. It is advisable to begin with passive movements and massage, then to proceed to resistance and active movements, and so on, but not to give up the treatment until the patient has become thoroughly engrossed in some hobby with outdoor exercise.

4. **The Bodily Deficient.**—In those who are mentally sufficient but bodily deficient, the instructor has the great advantage of intelligent help from the patient. Exercises must at first be simple and carried out slowly; the duration of the lesson must not be long, and plenty of rest should be given during it. At this stage, massage is of the greatest value. Later, the exercises involving increased rapidity of execution should be given. Slow movements affect the muscles most; rapid movements affect the nervous system most. Respiratory exercises, first passive, then both active and passive, and finally active alone, should be taught throughout. Short spells of drill are most useful in giving the young a good upright carriage, but must always be stopped as soon as the body begins to slouch. As the subjects grow stronger outdoor exercise should be encouraged. One of the best amusements is going for a "walk," which consists of a series of short sharp runs with periods of walking in between. By about the age of twelve or so, some outdoor sport, such as cricket, football, hockey, should be started. Many a boy would be much better and have a greater power of expanding his chest if respiratory exercises were taught and continued until growth practically ceases. Stress must be laid upon the great importance of treating these cases with rest as well as exercise. For instance, drill is excellent so long as a good upright carriage is maintained; as soon as the good position fails a period of rest should be enjoined.

The bodies and nervous systems of convalescents from general diseases are in an enfeebled state, and treatment should begin with passive movements and massage. As strength returns, active movements may be started and slowly increased in duration and work done, until the patient is restored to a vigorous state of mind and body. Convalescent or convalescing local conditions are treated in a similar manner. At first, reliance should be mainly placed upon the mildest form of physical exercise, massage, while exercises can be used later. When the local injury has affected a joint, or a joint has been more or less crippled with such a disease as osteoarthritis, exercise is most important in restoring and preserving functional activity.

5. **Mental Deficiency.**—Of recent years it has become clear that by means of physical culture and exercises a great deal can be done to improve deficient, backward, and imbecile children. This is the most difficult class of case for the instructor, who, it is most essential, should be specially trained and skilled in such work. The earlier in life that the training of the children can be commenced the better, but the lack of self-control renders this most difficult. A course of passive movements in the young and feeble-minded, perhaps combined with some electro-

massage, is often very beneficial. By means of repeated small advances and frequent repetitions improvement takes place. The satisfactory result does not come from mere improvement of muscular and general tone, but is due in part to the movements appealing to and educating the undeveloped brain through the muscular, tactile, and other senses. Many natural movements, particularly those of the arms, are inco-ordinate or choreiform in the feeble-minded, and like the inco-ordination of ataxy can be improved by re-educating the nervous system. Special attention must be paid to the position and habits of this class of children, as, being poorly developed muscularly, such deformities as scoliosis, kyphosis, or flat foot are likely to occur. It is very important to commence with the simplest movements, slowly, gradually, and with frequent repetitions, leading up to the more complex. The greater the mental deficiency, the more must the exercises be limited at first to the spine and trunk; the movements being slowly extended from the trunk to the limbs or periphery as the patient improves.

Physical exercises in the feeble-minded also have a moral effect. One of the greatest difficulties in teaching these patients is their waywardness and lack of control. Exercises are of great advantage in promoting control, thereby sowing the seed for the appreciation of and the submission to discipline. Instruction in eye movements seems to be of special importance in mentally deficient children, as the idea of number appears to be associated with them.

Insanity.—After the acute stages of insanity exercises may be very beneficial in aiding convalescence. It is important in these cases to start with some exercise with which the patient is already familiar, and of an automatic character, as such movements are the more easily relearned, and offer an obvious method of appealing to the nervous system.

6. **Abdominal Conditions.**—Exercises are useful in the treatment of various abdominal conditions, especially some forms of dyspepsia and constipation, while sluggishness and "congestion" of the liver are much relieved by abdominal exercises. Combined with abdominal massage these movements have been used for the relief of the symptoms of *enteroptosis.* In this way nutrition is improved, the subjective symptoms often become less, and by increasing the tone of the abdominal muscles the tendency of the various viscera to drop is lessened. The addition of fat during treatment, or its removal by treatment, also helps to restore the patient to a healthier condition. But as regards the mobility of the organs, little or nothing is directly accomplished. Treatment ceases, and when sufficient time has elapsed to undo the good which has been done, the patient becomes as bad as ever. The practice, adopted by many who carry out the art of exercises, of pulling on the movable kidneys is to be condemned, as more pain and discomfort are given to the patient than seems justifiable by the minute modicum of real good accomplished. The prognosis of this treatment of enteroptosis is good for immediate and temporary improvement, but bad as regards permanent relief.

The condition of the large bowel, found chiefly in middle-aged women, associated with pain along its course, diarrhœa or constipation, general loss of health, subacute or chronic appendicitis and so forth, to which the name of colitis is given, can be much benefited by abdominal massage and exercise. But the danger of the mild inflammatory condition of the appendix becoming acute must be carefully considered before adopting the treatment.

After abdominal and pelvic operations, and especially after draining local abscesses, a number of adhesions form. Exercise and massage are known to remove adhesions in the joints, and there is reason to believe that the same holds good in the case of the abdomen. Moreover, after an incision it is well to strengthen the abdominal walls by exercise, which will either benefit the scar, or cause a ventral hernia to form earlier than it otherwise would. If the latter is the case, the exercises will have given better tissues for suturing when closing this aperture.

For strengthening the abdominal walls about the inguinal apertures, youth and childhood are the times when this can be done directly. Later, but little is accomplished, especially if a hernia be present. But mere bulging of the abdominal walls above the inguinal canal can be much improved.

This brief account cannot be closed without some reference to the application of exercises to the diseases of women, first employed in 1861 by Dr. Brandt. It is natural that, as in other conditions, exercises may have a favourable influence on the subjective symptoms, relieve congestion and adhesions, and improve the general tone. But, unfortunately, as in so many specialties, too much is made of this with the result that the treatment may be abused by even honest enthusiasts.

For instance, the attention of the instructor is directed (by massage) mainly to influence the sphincter vesicæ, which in consequence becomes "more powerfully innervated," and incontinence of urine is (or may be) cured. The movements and massage can hardly be expected to do this. But it is known that conditions, as dysmenorrhœa, for which no cause has been found, have been greatly improved by trunk exercises without "internal massage." "Internal massage," given per vaginam or per rectum, has not been received favourably.

7. **Deformities.**—*Scoliosis.* Physical exercises have been used more for lateral curvature of the spine than for any other deformity. In fact, this is the only condition in which many know that exercises have any use. In consequence, the department is choked up with cases for which but little can be done. Surgeons are unanimous in the causation and treatment of lateral curvature; the usually accepted ideas of its origination are as follows:—

Primary lateral curvature: (i.) Congenital; due to the fœtus being in such a posture during intra-uterine life that its spine is bent laterally. (ii.) Acquired; rare.

Secondary lateral curvature: (i.) Due to muscular weakness and habitual bad position. (ii.) Due to disease of the spine. (iii.) Due to

disease or deformity elsewhere in the body, particularly of the legs or of the chest after an operation for empyema or a thoracoplasty.

Lateral curvature of the spine is in practice almost always secondary, being associated with muscular weakness, and the habitual use of bad position in standing, sitting, etc. Although a detailed account of scoliosis is out of place in this article, its causation must be considered. In the first place, the muscular weakness, though it favours, does not cause the curvature. The real cause is the habitual use of positions that curve the spine; when these positions are associated with muscular weakness, the natural curves cannot be removed when an erect attitude is assumed. Such attitudes have been called *asymmetrical postures of rest.* Then two factors come into play. First, the growing vertebræ must accommodate themselves to the new conditions, their bodies therefore become wedge-shaped. Secondly, the muscles on the concavities of the various curves possess a decided mechanical advantage over those on the convexity. These subjects have poor muscular development which is quite inadequate to restore the balance between the actions of the muscles on either side of the spinal column. Now consider the surgical teaching that these muscles must be strengthened by exercises. In a certain number of cases the deformity actually gets worse owing to the continuance or exaggeration of the physiological asymmetry or discord of the muscles of the back, and the continued growth of the spine which adapts itself to the curvature. It follows that those cases in which the curve can be rectified by the patient's own muscular action can be easily treated and cured; others in which the curve becomes obliterated by the use of certain positions and exercises, such as stooping, hanging, "spring-sitting," etc., can also be improved. But care must be taken that the muscles are exercised and improved in the corrected and not in the uncorrected position. If this is not done the exercise will strengthen the muscles on the concavity of the curve more than those on the convexity, so making the muscular asymmetry greater. In a third class the curvature cannot be completely obliterated, though it may be to some extent. These are the very cases in which the injudicious administration of exercise will make the curvature worse. Great care is needed in the treatment to avoid this, and prolonged rest on the back, and in such positions in which the curvature is improved, must be insisted on. This will enable natural healthy growth to do something to correct the deformity. Massage is given to the muscles of the back, and a few simple exercises can be taught in such positions as strengthen the muscles on the convexity of the curve. Special attention should be paid to active breathing exercises in the supine or prone position, and passive respiratory movements should be used for the side on the concavity of the dorsal curve. The movements are rather like those used in artificial respiration. In order to give them to one side in particular, only the arm of that side is moved; or if both are used, the one on the contracted side of the chest is pulled on most. This exercise may be improved by exerting traction on the leg of the opposite side at the

same moment that the arm of the contracted side is pulled. A few weeks of such treatment will do a great deal of good; whilst a few weeks of the injudicious use of exercises may do very great harm.

Kyphosis is an antero-posterior curve of flexion in the dorsal region of the spinal column. In children it may be due to some deformity or lack of expansion of the chest, or indirectly to general feebleness of body, and directly from the habitual use of slouching habits. In the young adult, it may also be due to a feeble condition of body and bad carriage of the shoulders. In the middle-aged it is usually the result of some position assumed in their occupation, such as a clerk bending over a desk, or a watchmaker. In the old it is almost always a natural condition. As the health and strength get less, the back becomes bowed, the shoulders round, and the head is carried less erect. This is probably due to bending of the spine caused by decaying vigour, and is followed by changes in the vertebral joints of the nature of osteoarthritis. More or less anchylosis eventually occurs. A very harmful change occurs in the chest with kyphosis. The expansion of the chest, upon which so much of one's daily vigour depends, becomes smaller, and the following complications ensue : embarrassment of the right side of the heart, deficient aeration of the blood, insufficient aspiration of blood from the veins, general venous engorgement of the viscera, and so on.

The preventive treatment in the young is very important. First, the strength must not be overtaxed, and a good position with erect carriage should be maintained during exercise, and bad habits avoided during rest. Secondly, let respiratory movements be taught. It will be remembered that the dorsal spine is flexed and extended during respiration. These and other exercises must be kept up for a long time, perhaps for years. The treatment for older patients should be directed to movements of the back. Respiratory and other exercises cannot do nearly the same amount of good in them, as the time of life when they can effect more than temporary good has passed by.

In the aged bowing of the back is natural as the bodily strength gets less. Hot-air baths, massage, and exercises will give some relief if the kyphosis gives trouble. But it is beyond human power to rejuvenate a worn-out frame.

It is advisable to postpone the stoop of the shoulders which occurs as age advances, because the chest then becomes flat, the sternum vertical, the ribs depressed, and there is no longer adequate movement with respiration. The right side of the heart is unaided, and the subjects suffer from palpitation and cannot take exercise. Chronic bronchitis soon begins and is rarely got rid of. The improper aeration of the blood is seen in the blue lips and nose.

Two other points deserve mention. Always exclude the existence of caries of the spine. Remember that though in rickets the curvature is a long sweeping bow, there is in bad cases an exaggeration of this bow resembling that of an angular curvature.

Lordosis.—By the term lordosis is understood an antero-posterior

curve of extension in the lumbar region of the spine. It is seen accompanying various diseases; the pathological subdivision of the cases. Examples are: diseases of the hip accompanied by flexion of the thigh, congenital dislocation of the hip, pseudo-hypertrophic paralysis. Another class is the anatomical subdivision of the cases. For instance, it is seen commonly in thick, short, strong men, who possibly adopt a superlatively erect carriage in order to make their stature appear greater. In weak or debilitated subjects pain may be experienced in the lumbar region. Thirdly, the physiological subdivision includes the pregnant woman and the man with a large abdomen.

The presence of lordosis should set on foot a careful examination into its causation, and treatment would be adopted according to the results obtained. If exercises are needful, those promoting flexion of the spine or trapeze work are the most suitable.

Deformities of the Feet.—This is not the place for a full account of the use of exercise for deformities of the feet, but a few remarks must be made about those of congenital origin. The commonest variety seen is that of talipes equino-varus, and the remarks to be made apply to it, though the principles will be equally applicable to other deformities. The first thing to bear in mind is that, in a baby, the tissues, even the bony, are growing, and that they can be moulded, just as a creeper grows to the wall and as a jelly fits the shape into which it is poured. Prolonged treatment by manipulations and massage are, therefore, indicated. The tendo Achillis should be gradually stretched and the foot turned from the varus to the normal position. Slow improvement will follow as the growth of the bones fits them to the new conditions. By the age of two years, when the child should be able to walk moderately well, it should have a foot upon the sole of which it can walk. If any tenotomies are performed it must be remembered that they will fail if not followed up by manipulations and massage; just as the operation for adenoids fails if not followed by nasal respiratory exercises. The mere walking on the sole will make it necessary for the bones of the foot to grow and adapt themselves to this position. In other words, the physiological activity involved in walking on the sole corrects an anatomical deformity.

Similar reasoning applies to many congenital deformities besides those of the foot. Cases of congenital dislocation of the hip or hips, if not bad enough for operation, can be taught to walk with a good carriage. More than this, if an operation is undertaken, it will fail in its object unless proper physiological exercises are taught afterwards. To gain their object all surgical operations for anatomical purposes must be followed by physiological exercises.

Conclusion.—As the health and condition of the body or of an organ can be improved by physiological activity, the therapeutics of physical exercises permeate the whole of the vast subject of the treatment of disease and defect. As they form the backbone of most medical and surgical treatment for cases which are not acute, it is impossible to

enumerate all the conditions benefited by exercises. This is especially difficult when the subject of exercise is divorced from that of massage. Massage itself is the mildest of passive movements, and entails the least expenditure of nervous energy, and is, therefore, the most valuable form of exercise for those who are or have been ill.

The divorce of massage and exercise may be shown by giving one instance of local weakness or deficiency. Lumbago is a typical example; yet how inhuman to begin treating the sufferer with exercises before rest and massage have assuaged his pain sufficiently. The use of physical exercises is for the weak and the healthy, rather than for those who are definitely ill.

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MASSAGE: TECHNIQUE, PHYSIOLOGY, AND THERAPEUTIC INDICATIONS

By J. K. Mitchell, M.D.

An endeavour will be made in the present article, not to consider the history of massage, but to give, simply and briefly, an outline of the technique sufficient to enable a physician to judge whether a masseur is well taught and works conscientiously; then to recapitulate the physiological effects which experimental studies have of late firmly established, to deduce from these its applicability in disease, and to indicate the diseases in which clinical experience has taught us its usefulness.

No doubt some of the distrust of massage has been due to the ignorance or incompetency of many of the professional manipulators, and to the absurd and extravagant efforts to proclaim it as an exclusive method of treatment. Unless inflammation be present, or some unusual tenderness or susceptibility, little direct harm, beyond discomfort, is likely to be done to a patient by rough or wrongly applied massage; but failure of any good result is harm enough. The practice of "mechanotherapy" by manipulators usually quite ignorant of medicine, certainly with no scientific training, and independent of proper diagnosis and directions from a physician, is altogether to be deprecated, and is one of the great sources of the prejudice against the method which still exists in the minds of many medical men. It is not necessary that such work should be undertaken by the practitioner himself—though this has been done in Germany and Sweden—but that he should be sure, if need be by personal observation, that the person he employs is well taught, industrious, conscientious, and obedient to orders.

The *technique of massage* is not difficult to acquire: and, as the whole value of the treatment lies in the proper execution of minute details, one who prescribes it should be familiar at least with the movements commonly used. "The various manipulations and their modifications naturally suggest themselves to one who clearly comprehends the anatomical, physiological, and pathological indications in any given case" (1).

With the exception of Granville's percussor, and the apparatus of the same sort belonging to the Zander system, no instruments among the hundreds devised for the performance of some of the movements can usefully replace the human hand. Great manual strength is not necessary, though a hand not too small is desirable; but very large and muscular hands lack the delicacy of touch which is so desirable. The most rational classification of the various movements is that into four kinds, for which the French names are usually, though not necessarily, employed, as follows: *Effleurage* (stroking), *pétrissage* (kneading), *friction* (rubbing), *tapotement* (percussion or striking). These may all be used lightly or strongly, deeply or superficially, and in various combinations,

as needful for special ends. Numerous other movements may be described, but all are in essence but modifications of these four cardinal ones.

Effleurage is performed with slow strokes, made with the flat or with the heel of the hand, or with its ulnar edge or with a finger only. The stroking should always be centripetal, the hand in the return movement only lightly grazing the skin. The chief usefulness of effleurage, apart from its slight stimulation of the skin-nerves, is in hastening the movement of the contents of the superficial veins and lymphatics.

Pétrissage—the most important and most difficult of the several movements—is done by grasping with the whole hand the tissues to be manipulated, lifting them somewhat, and kneading them with an alternate tightening and loosening of the hold. In large masses of muscle, like those of the thigh or calf, it is sometimes best to use both hands. The movement is very different from pinching. Care must be used that the skin moves with the hand over the underlying tissues. The surface hairs will be painfully dragged if the hand is permitted to slip over the skin. In certain favourable situations—in the upper arm, for example—the extended hands are placed upon opposite sides of the limb and moved rapidly backwards and forwards with firm pressure, rolling the muscle masses between them and pressing them together or against the bone. The effects are identical with those of ordinary pétrissage, but somewhat more stimulating from the greater speed of the manipulation. A slight contraction of the muscles is induced by pétrissage, the absorption of infiltrations in the tissues is promoted, their progress through the lymph-vessels assisted, the deep and superficial blood-vessels are stimulated, and the blood is moved with greater speed and in an increased quantity.

Friction is performed by firm rubbing in small circles with the thumb, finger-tips, or whole hand. It might well be included as a modified form of pétrissage, as it has precisely similar effects, and is useful where the tissues are too closely attached to bones to be picked up by the hand, as in the neighbourhood of joints; in such situations it is especially of value in the removal of articular effusions.

Tapotement is the application of rapid blows delivered with the ulnar edge of the hand, with the tips of the bent fingers, or with the flat of the open hand. The end to be attained and the tissue to be affected decide which method shall be used. It acts for the most part as a mechanical stimulant. If we wish to excite the peripheral skin-nerves we use the flat hand—for instance, in anæsthetic areas; to reach a nerve-trunk, blows with the finger-tips, rapidly delivered from the wrist (not using the whole forearm in a hammering fashion), are employed, and, to excite muscles, "chopping" with the edge of the hand, transversely to the long axis of the muscles.

Vibration is a form of tapotement, and probably its most useful form. The fingers, held extended somewhat firmly but not rigidly, or with all their tips brought together in a pyramidal shape, are placed upon the part to be treated, or the flat hand is laid upon it,— and then a vibratory

movement communicated to the tissues by the most rapid possible contraction of the forearm muscles. A vibrating apparatus, as is said above, can do this better so far as the small jarring motion is concerned, but a machine cannot measure or alter the applied force.

The French and the Swedish masseurs have wasted much ingenuity in subdividing the several manipulations with great subtlety, and some operators perform a great variety of what can only be called ornamental movements, fantastic flourishes and airy graces, like the affectations of a fashionable pianist.

In the consideration of the force and frequency of application desirable in any particular case, the usual direction to the student of massage must be remembered, namely, that his mind is to be given not to the movements his hands are making, but to the character and condition of the tissues upon which he is operating and to the effect that he wishes to produce. The force, therefore, must be such as to attain the desired end, and this will necessarily vary with the state of the tissues and the condition of the patient. In a chronic arthritis with firm exudation vigorous friction will be required; in a more acute trouble—a sprain, for instance—much less force will be needed; at first, certainly, only light effleurage. Nervous, hysterical, or excitable patients must be very gently handled at first and only for short periods. In certain cases (a recent sprain may again be cited as an example) massage three or four times daily will be of service, each application lasting only from five to fifteen minutes. Most massage procedures to be of use should be repeated at least once daily. General massage, such as is used for convalescent patients or "rest-cure" cases, must last from thirty minutes to an hour every day.

The usefulness of massage is greatly lessened by the common practice of employing some oily substance for lubricating the skin. Moreover, it is dirty; and the excuses offered, that, unless an oil be applied, the operator will pinch unpleasantly or will pull the hairs painfully, are confessions of incompetency. In old or much emaciated patients, whose skin is harsh, dry, and scaly, it is sometimes desirable to use an emollient; and for such purposes the best unguent is lanolin with the addition of enough oil of sweet almond to render it of the consistency of thick cream. Vaseline is difficult to remove satisfactorily after use; is not absorbed, and to some skins is irritating. Generally it may be said that no oily application should be used without the physician's orders.

There can be no question of the much greater value to the patient of massage when used directly upon the skin. Done through clothing, even the thinnest, the operator must fail in technique: the palpation of the tissue will be imperfect, and an additional amount of force must be used.

General massage is a form of passive exercise for those unable to take active exercise, or for whom active exercise is undesirable. It is usual, but not important, to begin with a lower extremity. The order commonly followed is legs, arms, back, chest, abdomen. The advantage of this is only in the small amount of movement required of the patient—and that the soothing effect of abdominal massage comes last and leaves the subject

lying on the back. If, for example, a patient is restless or chilly after massage in this manner, the order may be changed and changed again. After manipulating the foot, the leg is worked with kneading, stroking, and friction about the joints. It is best to put a sock or stocking on the foot when the massage is over; and every care must be taken to keep the parts warmly covered with a blanket as they are finished. After the legs the operator proceeds to the arms and treats them in the same way. In massage of the back vigorous, rapid, downward stroking over the spine is employed, as well as the treatment to the muscles. In rubbing the chest in women the breasts should always be left untouched. Last comes the very important operation of abdominal massage. In order to obtain relaxation of the abdominal muscles, the head is raised upon a pillow and the knees bent, while the patient is directed to breathe deeply. At first, especially in hysterical women, there is always a difficulty in overcoming the tension, largely involuntary, of the recti abdominales; but as the patients grow accustomed to the manipulation the muscles slacken. Deep friction in small circles, continued over the whole abdomen, is made first, using the fingers of one hand; then kneading movements, chiefly with the heel and palm, in a large circle round the navel; then similar applications are made over the large intestine, beginning at the right iliac fossa, and following the course of the ascending, transverse, and descending colon: the hands are placed on the two sides below the ribs and drawn forward with deep pressure several times; the region of the liver and the left hypogastric and hypochondriac regions are kneaded, reaching in this way the small accessible portion of the stomach, and the whole process ends by the operator grasping the abdominal walls lightly, but firmly, and imparting a rapid vibratory movement to them and to the underlying structures. Occasionally tapotement or clapping with the hand over the liver may be added to these procedures. After the completion of the massage the patient should be warmly covered and lie quiet for an hour. This hour of repose after manipulation is an important point, especially for persons not confined to bed. Unless it be insisted upon much of the effect of the treatment is lost.

The effects of general massage are very decided and apparent. The immediate results are a fine sense of well-being, a feeling of comfortable tiredness without exhaustion, and a pleasant drowsiness. In rare cases hysterical patients are aroused and excited by it; more rarely still, persons are found whom massage leaves chilled, irritated, and uncomfortable. In such cases the experiment may be tried of reversing in part the order of procedure, rubbing the abdomen first instead of last, then the chest and back, and finally the arms and legs. Occasionally it may be found that massage has been overdone, and that lighter applications are needed to give good results. Very seldom indeed do we find patients to whom massage is so disagreeable as to make its application entirely impossible.

The later effects are also well marked; the skin softens and shows a better colour; the appetite is improved as well as the digestion; the

bowels act more freely; sleep is more prolonged and sounder, and the muscles become larger and firmer. The results in cases of disease will be considered later in more detail.

Studies of the results of massage in health and in various maladies have been numerous and valuable in late years; the work of Bunge, Brown-Séquard, von Ziemssen, Weir Mitchell, Playfair, Sinkler, Gerst, Goodhart, Kleen, and Profanter, taking the subject from the clinical side, has been confirmed and wider possibilities for massage application have been suggested by the physiological experiments of several of these same observers, as well as by the labours of Lombard, Mosso, Maggiora, Lassar, Eccles, Glovetzky, Mosengeil, Mezger, Kronecker, Lauder Brunton and Tunnicliffe, Winternitz, and Zabludowsky.

The *immediate effect of massage* is to increase the amount of blood in the region rubbed; the skin is flushed, the vessels in the muscles receive a larger amount of blood, and the flow of blood is greater through the part for some time subsequently. Accompanying this there is a fall of general blood-pressure and a slowing of the pulse, if the manipulation has been a deep muscular stimulation. Superficial skin stimulation increases blood-pressure. An increased activity in the movement of the lymph-stream has also been accurately demonstrated.

It is obvious that we have here a useful indication for *the treatment of recent local inflammatory conditions*, such as result from sprains, dislocations, and the like. The increased circulation will not only prevent stasis and the migration of white corpuscles into the tissues, but will rapidly remove the corpuscles and lymph which have been already thrown out. Again, the secondary effect of the larger amount of blood passing through the region is valuable in case of any local disturbances of nutrition, indolent ulcers, undue amount of deposit following fractures, contusions, and myositis.

Donders, Pagenstecher, Damalix, Klein, and others have reported successes in the treatment of both *catarrhal* and *phlyctenular conjunctivitis*, *opacities* of the cornea, *pannus*, and even *cataract*, by means of massage. For full descriptions of their methods the articles by these and other ophthalmic surgeons must be consulted [*vide* References].

Besides these immediate effects other general consequences are perceived. One result of the changes in blood-pressure is an increased secretion of urine, another is that fatigue—whether local, as in an over-used group of muscles, or general—may be rapidly and pleasantly removed by massage, that is, by the removal of fatigue-products and by the flushing of the muscles and nerve-centres with quantities of fresh blood. Lombard, Mosso, Maggiora, and Zabludowsky have shown by experiments in their own persons, or upon animals, the prompt power of massage to restore functional ability to exhausted muscles. Maggiora found that this improvement did not take place in muscles whose blood-supply had been cut off. He further concluded that tapotement and friction were less effectual than kneading, and this again not so useful as mixed massage, *i.e.* the combination of the several movements as applied in

general massage; and that the beneficial effects of manipulation were, within certain limits, directly proportional to its duration. That more blood actually flows through the tissues during and after the rubbing has been proved by the careful experiments of Sir Lauder Brunton and Dr. Tunnicliffe. A series of clinical examinations of the blood before and after massage under very varied conditions of health and disease have recently been made by myself. Originally it was my intention to study the effects of massage in anæmia, but a wider field opened itself out as the very marked results in such cases appeared. In sixty observations upon thirty patients only three failed to show an increased number of red corpuscles after general massage. The conclusions reached were as follows:—In health massage increases the number of red corpuscles, and in less proportion their hæmoglobin value. In all forms and grades of *anæmia* there is a very large and constant increase in the number of red corpuscles after massage; this is greatest about an hour after treatment, slowly decreasing from that time. This decrease is, however, postponed further and further if the manipulation be daily repeated. There is an occasional but inconstant increase in the hæmoglobin value, an increase proportionately less great than that of the cellular elements. The increase in red corpuscles, estimated by the Thoma-Zeiss hæmocytometer, after an hour's massage was often as great as 20 per cent, and in some cases reached 50 per cent more than the original number observed. The increased activity of the superficial circulation is not enough to account for so great a change: moreover, if the increase arose merely from an addition to the number of red cells in the peripheral vessels at the expense of the rest of the circulating fluid, there should be an increase of hæmoglobin directly proportional to that of the red globules; yet in no case did the hæmoglobin-increment exceed 15 per cent, even when the corpuscular increase reached 50 per cent. It can scarcely be supposed that an hour's massage, much as it hurries the current in the vessels, can actually cause a greatly increased production of blood-corpuscles: although the repetition of treatment no doubt stimulates this process. Still, the effect of this new activity and movement of the cells upon metabolic processes must, at any rate for the time, be much the same as if a considerable addition were made to their number. Further, these examinations make it seem in every way probable that in health there are vast numbers of corpuscles ready for use if called for, and also probable that a part of the trouble in anæmic diseases may be a lack of availability or of activity in the corpuscles, that many of them are sluggishly lingering in the by-ways of the circulation, and only forced or pushed into greater activity and usefulness by the direct stimulus of massage. "The state of things in the system in anæmias may be, to draw an analogy from economic conditions, like the want of circulating money during times of panic, when gold is hoarded and not made use of, and interference with commerce and manufactures results."

Effusions of lymph or blood in serous cavities, in the substance of muscles, and in the sheaths of the tendons or nerves, may be removed by

means of massage. Reibmayr and Höffinger injected water into the abdominal cavity of rabbits, subjected some of the animals to massage afterwards, and on opening the abdomens found that in those which had been massaged the proportion of the fluid absorbed in a given time was more than one-third greater than in those not so treated.

Von Mosengeil made injections of Indian ink into two joints in rabbits, and massaged one joint. Upon examining the articulation treated, very little of the injected matter could be discovered in it, even when opened after only a few minutes' massage. The ink could be traced through the lymphatic vessels into the neighbouring glands. In the untouched joints the ink was found unchanged, no attempt at absorption having taken place.

Acute *arthritic disorders*, like rheumatism and gout, accompanied by general constitutional disturbance, are not suitable for massage until the acute stage has passed; but localised or traumatic arthritis and synovitis, and simple cohesion of joint surfaces where an articulation has been long unused in which there is no risk of promoting the resorption of toxic products, may properly be so treated. The results in sprains, *tenosynovitis* and the like, are sometimes amazing; and, if massage be instituted immediately, speedy recovery may be confidently predicted. The sooner after the injury manipulation can be begun the better. At first the swollen, bruised, and tender structures should not be touched at all, but effleurage made from the seat of the accident centripetally, to hasten the circulation from the congested part and help to carry off the exudation. Similar stroking should be used below the injured part, and, before the end of the application (which should last ten to fifteen minutes), it will be found possible to give effleurage and light friction directly to the inflamed tissues. At first manipulations should be made several times daily, and a firm bandage put on in the intervals.

Where we find old synovial inflammation with thickened connective tissue and firmly organised deposits, much more force may advantageously be used; and such a case presents one of the few occasions where the use of some unguent is desirable, since sufficiently strong friction frequently repeated on a small area will sometimes injure the skin unless a lubricant be applied.

Massage of the neck, in the form of downward stroking on the sides of the neck and friction and stroking from the occiput downwards, serves as a means of lessening the amount of the blood in the head by pushing onwards the venous flow. This manner of relieving cerebral congestion may be made use of for *insomnia*, where the activity of the brain is so great as to prevent rest, as it brings about that mild degree of cerebral anæmia which is the physiological condition necessary for sleep. Even where flushing, headache, sleeplessness, dizziness, and confusion of mind point to a *threatening apoplexy*, the same procedure is of service; and in migraine the effects are occasionally most happy. In the easily recognised complexus of symptoms somewhat loosely described under the vague name of "spinal irritation"—a state in which insomnia is frequently

very persistent—effleurage, vigorously applied, will be found a valuable aid in inducing sleep: here, however, it must be used upon the back as well as upon the neck. The technique of neck-massage is of the simplest. The operator, standing behind the sitting patient, lays the hands flatwise upon the lateral aspects of the neck below the ears, and pressing gently, strokes downward, over the jugular veins, at first with the ulnar edge of the hand, gradually turning the hand as it moves until the palm and then the radial edge carry on the movement. Pressure upon the hyoid bone and the larynx should be avoided.

Gerst has used the same means for the removal of the hyperæmia attendant upon concussion of the brain and upon fracture of the skull.

In *migraine, trigeminal and supra-orbital neuralgia, or neuritis*, much relief is felt from local massage; of course its use should not cause neglect of other measures, such as electricity, the regulation of the bowels and digestion, or remedies to combat accompanying anæmia. In migraine especially it will be found necessary to continue the treatment for some weeks to be sure of benefit. In these affections it is very common to see the masseur work from the centre of the forehead toward the temporal region, a violation of the maxim, stated above, that movements should be in the direction of the venous currents. Manipulation should follow the course of the frontal vein, from the temples toward the root of the nose.

Sciatica, whether we consider it as neuralgic or neuritic, is much helped by carefully applied effleurage. The German physicians prefer massage to any other treatment for this rebellious affection. Kleen's prescription is that as infiltrations (myositis in the gluteus maximus and medius muscles) frequently accompany or cause sciatica, careful palpation is to be made for these; and although, "on anatomical grounds, such infiltrations may readily escape the perception of the masseur, still the rule holds good . . . that energetic frictions should be made in this place, even if no pathological changes can be found. Furthermore, one should make vigorous tapotement with the fist along the course of the sciatic nerve as far as the hollow of the knee." Overstretching the nerve, by flexion of the thigh with a straight knee, pushed to the point of endurance, is, according to Kleen, to be added to the prescription.

Dr. Weir Mitchell has long abandoned these methods in obstinate sciaticas for a plan of his own which has been attended with remarkable success. To lessen the blood in the limb, and to remove the irritation caused by motion, the patient is confined to bed, the leg bandaged firmly from the toes to the groin with a flannel bandage, and the hip and knee joints fixed by a long splint from axilla to ankle, or, in patients who can be trusted to keep quiet, by sand-bags. The bandage is removed and the leg rubbed twice daily, general kneading of the muscles being used except of those near the nerve; even indirect pressure upon this structure is to be avoided. The nerve tract is to be "effleuréed" with long, steady strokes; the hip and knee joints passively flexed once or twice in a gentle manner, and the bandage reapplied. Three weeks

of this procedure will usually suffice for a cure, even in obstinate cases. Activity must be resumed gradually, and the use of the bandage and of a certain daily amount of rest in a recumbent position insisted upon for a time.

The treatment outlined for these neuralgias may serve to indicate the manner in which any form of neuritis or painful affection of a nerve may be handled by massage, whatever the origin of the disorder. The results of injuries, bruises, crushes, and even of sections of nerves are relieved by the same applications, though of course the methods employed will vary somewhat with the character and seat of the injury, and the stage of the disease. Manipulations cannot be begun upon wounded surfaces until skin-healing is complete. The atrophy of muscles consequent upon nerve-section can be minimised, the period of disability much shortened, the subsequent contractions prevented, and the danger of ultimate pressure upon the nerve by scar-tissue lessened. In old cases of wounds of nerves where contractions, joint-stiffening, muscle-atrophy, and the various disturbances of sensation have all appeared from neglect of early treatment, massage is indispensable. It may perhaps be necessary to repeat what I have already urged, that such a statement must not be construed to imply the neglect of other aids—douches, faradisation of the atrophied muscles and of the muscles opposed to contracted groups, galvanism to the nerves, the forcible breaking down of joint-adhesions, etc.[1]

Contracted scars, as from burns or other injuries, that have destroyed large areas of tissue may advantageously be subjected to the same manipulations as contracted muscles, though, as cicatricial tissue is but ill-supplied with blood-vessels, the results are less striking. Firm pressure, squeezing, pinching, kneading, and, where possible, stretching are the methods employed. Of course, the earlier the case is seen, and the less firm the cicatrices, the more successful the result, as the further increase of scar-tissue may be prevented, and that recently formed may be thinned and softened.

Writer's cramp and the allied forms of muscular difficulty, whether paralysis, tremor, or spasm from over-use of single groups of muscles, cannot be better combated than by massage and galvanism. The muscles usually affected are the flexors of the forearm or in the hand, and the occupations most commonly subject to the occupational neuroses are writers, pianists, telegraphists, watchmakers, stone-masons, or type-setters. The bicycle has of late given us a new form, in which the muscles of the thigh are affected; and one or two examples of an undescribed neurosis have been seen at the Infirmary for Nervous Diseases in Philadelphia in tram-car drivers, who are constantly pushing upon the hand-brake. Violinists sometimes suffer from cramps of the fingers of the left hand from over-use on the strings of their instrument; but in

[1] For detailed cases of such disorders and their successful treatment by the means suggested the well-known work of Dr. S. Weir Mitchell on *Injuries of Nerves* may be consulted. The present writer has reported the later history of a number of Dr. Mitchell's cases in *Remote Consequences of Nerve Injuries and their Treatment*. Philad. 1895.

such cases there is often a neuritis of the terminal filaments present also. In all such disorders absolute rest of the affected part is the first requirement, and massage the next. Authors differ as to the proper technique, but probably the most effectual method is strong stroking and kneading, followed by percussion to the affected muscles and to their nerves where these are accessible. In instances where muscular infiltrations are found in connexion with these palsies, or where neuritis is present, especial attention must be given to the parts thus affected.

Torticollis, when rheumatic in origin, yields readily to massage of the affected muscles if applied early. When once established the disorder is very obstinate, and should be treated by forced passive movements of the affected muscles and the cultivation of their opponent groups. When the cause lies more obscurely in an affection of the cervical portion of the cord, massage is of less use, though it helps to relax the spasm, and may be of important service by strengthening the opposing muscles.

An excellent instance of the difficulty with which a new systematic treatment of disease makes its way is furnished by the facts concerning the application of massage in *chorea*. Blache in 1854 presented to the Académie de Médecine in Paris a report of 108 cases of chorea successfully treated by massage, and for a time the method was fashionable, and has continued in use in France to a certain extent; but the majority of medical men continue to rely upon drugs, with a confidence unimpaired by the fact that no matter what or how much medicine be given the clonic movements continue for weeks. In the lesser degrees of chorea minor, arsenic, iron, fresh air, and proper feeding may be sufficient. In the more severe cases, even omitting the consideration of chorea major, bed, with massage, will be found to effect a very rapid and usually perfect cure. As the co-ordination improves, and the involuntary jerkings lessen, cautiously increased, slow gymnastic movements should be added. Besides its influence over the muscles general massage is of value in counteracting the anæmic or chlorotic condition so commonly associated with the disease. Drs. Goodhart and Phillips, in their series of cases of chorea treated by massage, rather understate than overstate the favourable results.

In the treatment of many other disorders of the central nervous system massage has a recognised and well-established place. In *acute anterior poliomyelitis* it is at least helpful in maintaining nutrition. Sir William Gowers, Prof. Eulenberg, and others describe improvement in cases of *pseudo-hypertrophic paralysis* during its use. In the early stages of this disease it has certainly been my good fortune to see arrest of the progressive paralysis and a decided increase in the strength of the weakened muscles.

In *locomotor ataxia* the effect is often astonishing, although one should remember that periods of arrest, even of improvement, occur in this disorder without treatment. But the results exhibited appear too consistently in case after case to be the result of a fortuitous coincidence of the "normal" cessation of activity in the degenerative process with the beginning of treatment by massage. Patients with ataxia usually suffer

less pain if active exercise is restricted; and the mechanical treatment is useful in overcoming the ill-effects of this inactivity. Yet this alone would not account for all the improvements; the anæsthesia and paræsthesia disappear or lessen, as well as the lancinating pains; the insomnia, so often present, is alleviated; even the difficulties of defæcation and micturition diminish. Recovery is not to be looked for—no power can renew degenerated nerve-cells—but in a large majority of cases decided improvement may be confidently expected.

Persistent kneading, stroking, and tapotement of the paralysed parts will do much to restore function in muscles palsied by *anterior poliomyelitis*, and massage and faradism should be continued in such cases for a year at least before giving up to despair, even if there be no apparent improvement in the muscles. The local temperature, usually very low, can always be raised several degrees by massage, and even if the muscular tone and voluntary movement are not restored, the increased activity of the circulation, which can be established by persistent effort, will make a great difference in the patient's comfort. Active treatment should be kept up as long as even the smallest degree of gain in power is made.

In *paralysis agitans* the ache and numb soreness of the overactive muscles is relieved by massage. Sometimes the tremor will be greatly lessened by massage, and when this occurs massage should precede the more useful treatment by long-continued voluntary movement exercises, with which the patient is taught the relaxation of the contracted muscles, to walk with a free step, to hold himself erect, and to overcome gradually the stoop and the festination characteristic of the disease.

In *cerebral birth palsy* (congenital spastic paralysis) similar useful effects are secured by massage followed by precision exercises.

The direct influence of massage upon nutrition, the peripheral circulation, secretion, and excretion, the indirect effects upon the heart and upon respiration, combine to render it a most important aid in treating the protean aspects of *hysteria and neurasthenia*. Individual aspects of each case, in the way of sensory disturbances, disorders of digestion, and the like, may require special modifications in the application of massage; but for the most part what has already been described as "general massage" will be found the most useful. Combined with rest, full feeding, and isolation, it is an indispensable part of the "rest-treatment" of Weir Mitchell (13). For the details of the application of these means the original essay in which it was proposed may be consulted, or the late Dr. Playfair's book (14), by which it was introduced into England. Care must be taken at first not to overwork patients; but after a few days massage may be ordered for a full hour daily, or even, as Dr. Playfair used it, twice a day. Especial attention should be given to the proper and thorough performance of abdominal massage, on which much of the patient's ability to take and digest food, as well as the regularity of the intestinal action, will be found to depend. A weekly weighing of the patient will tell whether massage is properly performed or not. If weight is not being gained some oversight will be found, usually either

that the diet is insufficient or imperfect, or the massage ill performed. Dr. Playfair was of opinion that the desire for food and the power to assimilate it are the best guides as to the efficiency of the rubbing. Another indication will be found in the urine, where the presence of deposits of urates or uric acid will quickly tell of mal-assimilation.

Patients with *melancholia* and various forms of *insanity* may advantageously be rubbed should the general indications call for it. Those who refuse to take active exercise, or if forced out of doors drag listlessly about, often need it. Melancholia, occurring about the time of the menopause, has many of its most disagreeable symptoms greatly mitigated by massage; for instance, the flushing so often complained of in various forms is improved by the better balance of circulation which is brought about by manipulation.

Massage for gynæcological purposes is a matter for a special treatise—at least so far as the direct manipulation of the uterus by Brandt's method is concerned. Its desirability is open to very grave doubts, although its utility seems to be established by the testimony of Profanter's reports of Schulze's cases (15), Bunge's articles, and the studies of Reeves Jackson of Chicago. These authors have described successes in the treatment of the various forms of displacement of the uterus and its appendages, of hyperplasia, of chronic metritis, and most decidedly of pelvic exudates, para- and peri-metritis.

The technique consists in raising the uterus (and, so far as may be, its appendages) by a finger of the left hand in the vagina, by which it is held against the abdominal wall, where it is kneaded and pressed upon by the right hand. That such treatment may be of great usefulness in the removal of old inflammatory deposits, and restore tone to the uterine walls and to the ligaments, is evident from the effects of like manipulations elsewhere. Pregnancy, acute inflammation, and of course the presence of catamenia, are contra-indications. Further, it is obvious that such treatment should only be entrusted to a physician, whether man or woman; and whatever the results may be, it is so tedious, fatiguing, and unpleasant to the performer, so annoying and painful to the patient, and open to so much abuse, that it is little likely to find favour.

Massage, in conjunction with other and more usful measures, may be applied to the reduction of obesity. Dr. Weir Mitchell, Dr. Goodell, and others have used it, together with a minimum quantity of food, to reduce the unwholesome adipose deposits of that very troublesome class of patients, the fat anæmics. By keeping them quiet in bed and giving nothing but skim milk in small amounts, weight may be rapidly and safely lost. [*Vide* art. on "Obesity."] Unusual or excessive local accumulations of fat may be removed by massage limited to the abnormal areas, and used with considerable vigour at short intervals.

There is a remarkable unanimity of opinion among those who have used it as to the value of massage in the *morphia habit*, and the other forms of drug addiction. It should be used throughout the course of treatment whatever be the plan employed, and with especial care during

the collapse which almost inevitably follows a sudden withdrawal of the accustomed stimulus, be it opium, cocaine, chloral, or alcohol. The weak heart calls loudly for help in such patients, especially in the slaves of morphia; and as the stomach is apt to be very irritable, it is an advantage to have this means of strengthening the movement of the blood without risk of upsetting a feeble digestion. Moreover, it has a remarkable sedative effect, due in part, no doubt, to the resulting relaxation of the peripheral vessels and in part to its soothing influence upon the irritable nerves.

Though the conditions which render massage undesirable or impossible are implied in much that has already been said, a few words on the *contra-indications* may be added.

Acute skin inflammation, burns, unhealed wounds, in fact any break in the cutaneous surfaces, render the use of massage impossible, at any rate upon the affected locality; although, as has been stated, it may sometimes be employed in the neighbourhood for its derivative effects.

The presence of fever should act as an absolute prohibition, as the manipulation causes a rise of temperature. Treatment may in certain cases—in consumptive patients, for example—be used in the afebrile interval.

In all processes in which pus is formed, as well as in cases of malignant tumour, it is obviously undesirable to apply a means which may result in the dispersion of infective products into the tissues or throughout the system.

Weakened vessel walls from general causes, fragility of the arteries, or dilated veins, forbid deep kneading, though effleurage may be employed.

Pregnancy contra-indicates abdominal massage, though no hesitation need be felt in using muscle-kneading, and friction to the rest of the body up to a very late date in the period of gestation.

John K. Mitchell.

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J. K. M.

THE MEDICAL APPLICATIONS OF ELECTRICITY

By H. Lewis Jones, M.D., F.R.C.P.

Electrical currents are used in medical practice for purposes of treatment, and as an aid to diagnosis in diseases of the nervous system. They are also used for the production of Röntgen rays, which have many useful applications in the fields of diagnosis and of therapeutics. Since the discovery of the Röntgen rays their applications to medical purposes have been so largely developed that they will be considered in a separate article of this work.

Electricity is also used for the heating of galvano-cauteries, for the illumination of exploring lamps, for the energising of the electro-magnets used in ophthalmic surgery, and for the production of the various forms of concentrated light which are used for therapeutic purposes.

When electricity is directly applied to the human body, it is usually employed in the form of currents from voltaic batteries, or from small induction coils, and is used at a comparatively low pressure, but in certain forms of electrical treatment, viz. in electro-static applications, and in the case of high-frequency currents, the pressures employed reach many thousands of volts. The electric lighting mains have also been brought into use for medical purposes by the help of safety resistances and other devices, so that every requirement of medical and surgical practice can be met by the use of current from the main, without the need for batteries.

There is no manner of doubt that electrical currents produce definite physiological effects; from a consideration of these it is possible to arrive at an estimate of the value of electricity in the treatment of disease, and medical electricity may be defined as the application of our knowledge of these physiological actions to the study and treatment of disease. The effects produced by electrical treatment may be arranged thus:—

Physiological Actions.—*Stimulation.*—Electricity acts as a stimulus, not only upon the contractile tissues, both directly and through their motor nerves, but also upon the sensory nerves, and through them upon the central nervous system. It also influences the vasomotor system. These vasomotor influences of electric currents can be made to play an important part in the relief of the pain and congestion which occur in many morbid states. A very large part of the good effects of electricity in disease may be ascribed to the stimulation which electrical applications produce. All living tissues are stimulated to greater activity by electrical currents, particularly when the currents are variable. D'Arsonval has shown that under the action of a varying current the metabolic processes of the body are increased, even if there be no muscular contraction set up, so that the

effect is not merely secondary to the muscular contractions produced by the treatment.

The improvement in health shown by rickety children, and by anæmic and debilitated persons when they are treated by general electrification with varying currents is conspicuous; they increase in weight, and eat and sleep better.

These effects are to a certain extent shared by other methods of stimulation, as, for instance, by massage, by hot and cold douches, and so forth; but electricity has certain advantages over these other modes of stimulation, from its greater effect in setting up active muscular contractions, from its power of penetrating and traversing the tissues, and from the ease with which it can be directed to any particular part, and can be regulated as to strength.

The effects which peripheral stimulation exerts upon the central organs, and through them upon the periphery again, may sometimes play an important part in electrical treatment, and may afford an explanation of the benefits which follow in cases, such as hemiplegia and infantile paralysis, where the treatment has been applied to the peripheral parts only, although the lesions concerned are central.

Electrotonic Effects.—The physiological effects of electrotonus have been used as a guide in treatment. With alternating or interrupted currents electrotonic states cannot be expected, but with constant currents the phenomena of electrotonus should be kept in mind in treatment, for they show when the exciting action of the exalted irritability of kathelectrotonus is to be brought to bear upon a part, as in paralysis; and when the calming effects of the diminished irritability of anelectrotonus are more desirable, as for the relief of pain and spasm. It is difficult to assess the value of electrotonus in electrical treatment, as it has not yet been proved to be of any special value.

Electrolytic Effects.—Another effect of electric currents is electrolysis, which is made use of in surgery when caustic effects are desired, as, for example, in the destruction of nævi, and the removal of moles and of superfluous hair. In the more purely medical applications of electricity, these destructive electrolytic effects must be remembered in order to be avoided, but the phenomena of electrolytic conduction involve not merely the separation of chemical compounds into their elements, but also the setting in movement of the positive and negative ions of the electrolyte towards the positive and negative poles. The electrolyte in the case of the human body is the whole mass of the saline constituents in solution in the juices of the body, and the passage of a current necessarily produces changes in the distribution of the ions along the whole path of the current. The variety of the saline constituents of the body is great, but the most abundant of them is sodium chloride. In order to simplify the consideration of the migration of the ions we may for the moment regard the juices of the body as a dilute solution of sodium chloride of a strength of five parts in a thousand. When a current is passed through the body by means of electrodes of metal, the chlorine

ions of the electrolyte begin to move towards the anode. On arriving there they part with their charges and tend to be liberated as chlorine, but owing to secondary reactions they may enter into fresh combinations there, setting free HCl and oxygen, or uniting with the metal of the anode to form chlorides, oxides, or oxychlorides. The sodium ions near the anode are repelled and migrate inwards towards the kathode. At the kathode the sodium ions are attracted and tend to appear as metallic sodium, but owing to secondary reactions the products actually set free there are sodium hydrate and gaseous hydrogen, and the corresponding chlorine ions are repelled and migrate inwards to reach the anode.

It is to the secondary chemical products of electrolysis that the caustic effects made use of in surgery are due.

In the case of the ordinary electrodes used in medical treatment, the separation of the products of electrolysis takes place in the moist chamois leather or other water-bearing material with which they are covered. These coverings, in fact, are made use of to absorb the chemical products, in order to protect the skin from their action.

Diffusion, however, plays its part, so that with prolonged applications, especially if the density of the current is great, the chemical products of the electrolysis may make themselves evident by exercising their proper chemical action upon the surface of the skin, and burns may thus be produced in the course of electrical applications.

The passage of ions into the tissues from the moistened electrodes or from their coverings has been observed by experiment, and has been used for purposes of treatment. The ionic movement is quite distinct from that of osmosis or of simple diffusion, as is shown by an experiment of Leduc, who connected two rabbits in series by means of a pad soaked in saline solution. On applying an anode moistened with strychnine sulphate to the skin of the first rabbit, the kathode moistened with a similar solution being applied to the second animal, he found that only the first rabbit was affected by the alkaloid, which migrated into its body from the anode, while the second animal remained unaffected during the time of the experiment, the ions migrating into its body from the kathode being harmless SO_4 ions. When the experiment was repeated with cyanide of potassium, the rabbit at the kathode was poisoned, the toxic constituent of the chemical used being the ion of cyanogen, an anion or positive ion, migrating inwards from the kathode only.

To employ electricity as a means of introducing a drug into the body may seem to be a needlessly complicated method, and it may be thought that the methods of giving drugs by the mouth or by the hypodermic syringe are both simpler and better; still there are some special objects which can be conveniently secured by the electrolytic method, as, for instance, the introduction of cocaine to produce local anæsthesia. This procedure is of value for small superficial operations, and it has quite recently been recommended by Sir William Gowers as a remedy for the superficial pains of locomotor ataxy.

It is not quite legitimate to assume that the effect of ions electrically introduced is identical with that of the drug administered by the ordinary methods. By electrolysis the ions may be forced into the actual cellular constituents of the body, whereas a drug circulating in the blood after administration by the mouth may not always gain entrance into the cells of the body, even if it be present in the lymph which bathes the cells.

Electrolysis may also be used for the purpose of extracting from the body such ions as are injurious. In France, Bordier has introduced lithium into the system of a gouty patient by the use of an electrolytic bath containing lithium chloride, and he further claims to have been able to detect in the bath, at the end of the operation, a certain amount of uric and oxalic acids, which appeared to be derived from the tissues of the patient by the transport of anions of these bodies towards the positive pole.

Electric Osmosis, Cataphoric Effects.—In addition to the migration of ions in an electrolyte under the influence of the passage of a current, there is also a movement, *en masse*, of the solution in the direction of the flow of current, namely, from the positive to the negative pole. Fluid can be made to pass in this way through membranes or porous diaphragms against the force of gravity, and it has been proposed to make use of this effect as well as that of the transportation of ions for the introduction of drugs into the body. Recent work seems to show that the migration of ions is the more important factor of the two, and perhaps is the only factor worthy of consideration in practical electrotherapy.

Units of Measurement.—It is impossible to have clear ideas upon medical electricity unless the meaning of the words Volt, Ohm, and Ampère are understood. These terms stand for the units in which electrical quantities are expressed, and are as necessary to the subject as are the better known units of measurement, such as the inch, the pound, and the pint, to matters of everyday life. The *volt* is the practical unit of electro-motive force, or electrical pressure ; and the electro-motive force of a battery expresses the tendency of such a battery to produce an electric current, just as the pressure in a steam-boiler expresses the tendency of the boiler to emit steam. In the former case the closure of a conducting circuit, and in the latter the opening of a valve, are necessary before the discharge can actually occur.

The *ohm* is the practical unit of resistance, and is necessary because electrical conductors differ from one another in their conductivity ; those which conduct well are said to have a low resistance, and those which conduct badly are said to have a high resistance. Metals are good conductors ; among metals silver and copper have the least resistance. The resistance of a wire or rod or other mass of any substance depends upon the specific resistance of the substance, and it also varies directly as its length, and inversely as its sectional area or thickness : thus a long or a thin wire of copper will have a greater resistance than a short or thick one.

The *ampère* is the unit of current, and the three units are so related to one another that an electro-motive force of one volt acting upon a conductor whose resistance is of one ohm will set up in that conductor a current of one ampère. This relation, known as Ohm's law, can be expressed, in symbols, by $C = \frac{E}{R}$, where C stands for current expressed in ampères, E for electro-motive force in volts, and R for resistance in ohms; if two of the three quantities are known the third can be calculated from them; thus when an electro-motive force of 12 volts acts upon a resistance of 8 ohms, the formula $C = \frac{E}{R}$ gives us, by simple substitution, $C = \frac{12}{8}$, or $C = 1{\cdot}5$ ampères, which is the resulting current.

As a current of one ampère is never applied to patients in ordinary medical treatment, the thousandth of an ampère (·001 ampère) or *milli-ampère* forms a more convenient unit, and medical currents are usually expressed in milliampères; thus five milliampères is a magnitude of current commonly used in treatment, and it is more easily expressed in that way than by the fraction ·005 ampère.

The resistance of the body is high, very much higher than that of a metal; and it varies considerably with the moisture or dryness of the skin: under conditions of medical treatment with wetted electrodes, it may be taken as ranging between 1000 and 5000 ohms. It is worth while to calculate the electro-motive force necessary to send a current of five milliampères through such a resistance. First, in the case of 1000 ohms—

$$C = \frac{E}{R} \quad \therefore \quad RC = E, \text{ or } E = RC.$$

$$\text{But } R = 1000 \; C = {\cdot}005 \quad \therefore \quad E = 1000 \times {\cdot}005 = 5 \text{ volts.}$$

Secondly, in the case of 5000 ohms—

$$E = RC = 5000 \times {\cdot}005 = 25 \text{ volts.}$$

A medical battery must, therefore, have an electro-motive force of 25 volts if it is to drive a current of 5 milliampères through a body whose resistance is 5000 ohms.

The cells usually supplied in portable batteries have an electro-motive force of 1·5 volts per cell, and 30 cells (a usual number) properly connected together have a combined electro-motive force of 45 volts: this gives an ample margin, and would send a current of 15 milliampères through a resistance of 3000 ohms. As this current is not often exceeded, and as, by thoroughly moistening the skin, the body resistance can usually be brought well within 3000 ohms, this number of cells is sufficient. Beyond this the weight and cost of the battery increases out of proportion to its efficiency.

The Medical Battery.—In choosing a battery for medical purposes the essentials are to have one which is efficient and does not require frequent attention. In many cases it is necessary to carry a battery to the houses of patients, therefore portability must not be lost sight of. Medical batteries, consisting of from 25 to 40 cells arranged in a case, and fitted with commutator, current collector, galvanometer, and induction coil, are sold by the instrument makers. This arrangement is commonly called a "combined battery." These are quite suitable for testing the reactions of nerve and muscle, for general medical application, and for electrolysis. The cells used are either small Leclanché cells or "dry" cells.

FIG. 6.

Owing to their small size their capacity is not large, and they cannot long give out large currents without becoming exhausted, but with proper care they may be counted upon for twelve months of steady work for all ordinary purposes of testing and treatment, including occasional use for the electrolysis of nævi, an operation which demands fairly large currents. After that time they will require recharging or renewal. It is best to use small dry cells, and to discard them altogether when exhausted. The dry cells cost only about eighteenpence each. For working the induction coil in portable medical batteries one or two separate cells of larger size are fitted; these run down more rapidly than the others, and may require renewal more frequently, and they should be so placed in the battery as to be easily reached for this purpose. Catalogues may be consulted by those wishing to purchase a medical battery. The details of the fittings

of portable batteries vary with the different makers, but instructions for use are usually supplied with the instruments.

When the electric light mains can be used, a home installation for medical purposes can be arranged, which will render a battery of voltaic cells unnecessary. For details of these equipments the reader should consult special text-books.

There is no particular advantage in having a fixed installation in the consulting-room as well as a portable combined battery, for the latter will serve at home as well as in the houses of patients, and as all battery cells tend to deteriorate in time whether they are used or not, there is twice the cost of maintenance with two batteries that there is with one. Naturally it is sometimes convenient to have a fixed installation at home, as well as a portable apparatus; but it is more economical and less troublesome to have few batteries.

Although it is in many ways a convenience to have the coil and the battery of cells combined in one instrument, the medical man is likely to find it convenient to have a separate portable induction coil, as the possession of such an instrument may sometimes obviate the need for carrying about a heavy combined battery. So, too, one may obtain simple batteries of cells arranged in boxes at low prices, which are often useful when it may be desired to lend a battery to a patient. For details of these batteries the instrument makers' catalogues should be consulted.

Continuous and Interrupted Current.—A portable battery of the kind just described can be used for applications of so-called continuous current and of interrupted current. In some instruments a switch is provided, and in others a distinct pair of terminals is fitted, in order to allow the operator to make use of either kind of current at pleasure.

The terms "continuous current," or "constant current," or "galvanic current" are applied to the current of the cells of the battery, and the current furnished by the induction coil is known as the interrupted or faradic current. The current from the cells of the battery flows through the circuit in one direction from the positive to the negative terminal so long as the circuit is closed, and if the resistance of the circuit remains unchanged its strength is uniform, and when the circuit is broken by removing the electrodes from the patient or by opening a key, the current ceases abruptly. If the electrode be caused to slide over the surface of the body there will be variations of strength in the neighbourhood of the moving electrode; for the point of entry of the current, or point of greatest density of flow, will vary in position, even though the total current flowing in the circuit, as indicated by the galvanometer, be steady and uniform.

Thus the "continuous" current may be applied either in the form of a steady flow, as its name would naturally imply, or in a series of impulses produced by the operator by means of some circuit-closing or circuit-opening device; or, again, the current through any particular part can be made to vary in a gradual manner by means of the sliding movements of the electrodes, as already described. In all of these forms

it is still spoken of as the continuous current, for purposes of convenient description, and to distinguish the current of the cells from that of the induction coil.

The current of the induction coil is of a different character. It consists of a series of impulses or waves of current which follow one another in rapid succession, a common rate or "frequency" being one of forty or fifty impulses per second. In medical practice the induction coil has been universally adopted as a source of interrupted currents because it provides a very convenient means of producing marked sensory and motor effects at a small cost. For purposes of stimulation it serves admirably, and in so far as electrical treatment consists of the simple stimulation of living tissues, the induction coil is a most valuable appliance. Its use for accurate work, however, has the drawback that the measurement of induction-coil currents is impossible in practice with any certainty.

In its simplest form an induction coil consists of a coil of insulated wire wound upon a reel or bobbin with an iron core, and provided with an arrangement, usually a vibrating spring, for automatically closing and opening the circuit. It is connected to a voltaic battery whose current passes through the interrupter, and the current is thus periodically established and interrupted in the windings of the coil. With every make and break of contact the magnetic field of the apparatus is caused to vary, and currents are induced in the wire coil. The induced current at break can be led off by properly arranged conductors, and was named by Faraday the "extra current." In medical parlance it is generally called the "primary current." The primary current is a series of electrical impulses or waves, all passing in the same direction, and corresponding in time and frequency to the interruptions of the battery current; each wave is due to a sudden rise and fall of electro-motive force in the wire, the whole time of each wave being a very small fraction of a second, and varying considerably in different coils.

The secondary current of an induction coil, as its name suggests, is derived from a second entirely independent coil wound upon the same bobbin as the primary coil. Being in the same magnetic field as the primary coil, it is acted upon in a similar way, but the effects produced in it are not quite the same. In the secondary coil there is an induced electro-motive force corresponding to the rise of magnetism and an opposite electro-motive force corresponding to its fall. Both of these can give rise to currents through an external circuit, and because they are in opposite directions the currents from the secondary coil are said to be alternating. The two semiphases are not exactly alike in all respects, although the total flux of electricity is the same in each, for the electro-motive force set up at the "make" of the primary current is lower than at the break, and the duration of the wave is longer, because the rise of the magnetising current in the inducing coil is more gradual than its fall. The electro-motive forces developed by induction in the secondary coil vary very much in different instruments. They may reach maxima

which are higher than that of the battery which supplies energy to the apparatus.

The properties of the discharges of an induction coil are modified by the number of turns of wire in the secondary windings. A coil of few turns (two or three hundred) has a lower electro-motive force and a lower resistance than a coil of many turns (two or three thousand); and besides its resistance there is another factor which increases with the number of turns, and is known as its self-induction: this retards the rate of rise and fall of current in the coil, and diminishes the magnitude of the current which can be taken from it. Thus a coil of many windings has a high electro-motive force so long as very small currents are taken from it, but this falls rapidly when the resistance of the external circuit is low; a short coil has a lower electro-motive force, but is capable of giving a proportionately larger current without fall in its electro-motive force. For treatment with moistened skin and wet electrodes a long coil is not needed, but for the stimulation of the superficial cutaneous nerve-endings with a dry skin and a wire brush—a method sometimes adopted—a long coil is needed, as the dry skin has a very high resistance, and requires a high electro-motive force to drive through it even the small current required in this mode of treatment. Some medical coils are therefore provided with two interchangeable secondary coils; but the same advantage can be had from one coil, if its windings can be tapped so as to use either a part or the whole of it at will.

Duchenne long ago maintained that the physiological effects from long secondary windings were not identical with those from short windings. At that time electrical science could offer no explanation of this. It was suggested that the difference was a matter of electro-motive force, which is greater with a long secondary. This did not satisfy Duchenne, because the differences observed by him were independent of the mere strength of the electro-motive force or current. Differences in these points may be adjusted, and were adjusted by him, but the innate differences in quality remained, in spite of adjustments. The essence of Duchenne's contention was this, that the ratio of motor to sensory effect was not identical in the two types of secondary coil. With long coils the sensory effects were strong at weak degrees of motor effect, with short coils sensory effects were weak at strong degrees of motor effect.

The accompanying tracings of the secondary discharges of induction coils throw light upon the differences observed by Duchenne. They show that the durations of the impulses are longer with long secondary windings than with short, and that the presence or absence of the iron core has an even greater effect than the length of the wire windings. Fig. 7 is a tracing of the secondary current of a very short coil with the iron core removed. Fig. 8 is that of a long secondary coil without iron. Fig. 9 that of the same coil with the iron core inserted. Fig. 9 further shows that when the rate of interruptions is rapid, the slowing effect of the iron core has the effect of producing interference of the current waves,

so that neither of the curves is completed when the succeeding wave commences.

These tracings enable us to understand the differences in quality of current which different induction coils may present. The inequality of the impulses at make and at break, the unknown duration of the intervals between successive impulses, and the not uncommon irregularities of the vibrating hammer interrupter, make the induction coil an unsatisfactory instrument when exact work is required.

When the question of the use of interrupted currents in diagnosis is examined, it is found that there is no reason why interrupted currents from other sources should not be employed. S. Leduc has recently drawn attention to this matter in a very instructive paper, and has shown

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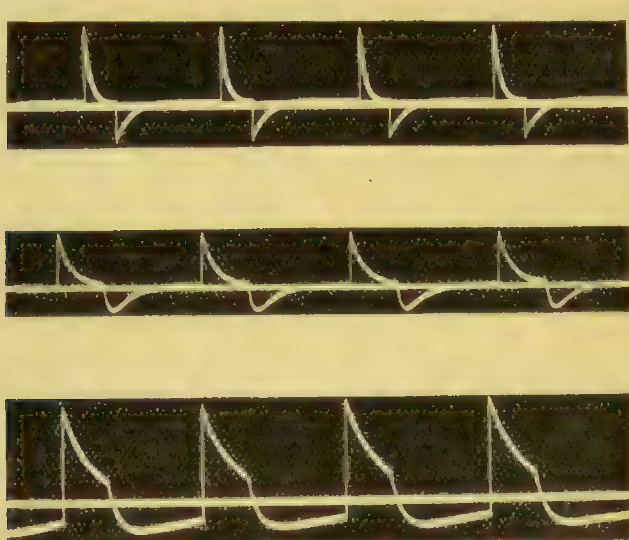


FIGS. 7-9.—Current Curves of medical Induction Coils.

that by the use of a continuous-current source and a mechanical interrupter it is possible to produce all the effects upon nerve and muscle which have hitherto been specially associated in the minds of medical men with induction-coil currents.

The advantages of Leduc's method are considerable. The current of his apparatus is uniform, and it can be accurately measured, the frequency of the interruptions can be regulated, and the duration of the individual impulses can also be regulated. Finally, the painful effect upon the patient can be made less than it is with most patterns of induction coil. In time all exact diagnostic work in the testing of nerves and muscles will be done by means of an apparatus of the kind devised by Leduc, and the use of the induction coil will be abandoned except as an instrument for rough and ready purposes.

The mechanical interrupter used in Leduc's apparatus consists of a commutator driven by a small electric motor. The segments of the

commutator, in their rotation, alternately make and break the circuit through which the current is conveyed to the patient. By means of certain simple modifications the commutator can be arranged to give a series of impulses in one direction, or the impulses may be made to pass alternately in opposite directions. In the former case the current will be a simple interrupted current, and in the latter it will be interrupted and alternating.

Sinusoidal Currents.—The dynamo machine has provided therapeutics with a new form of electrical current, which has valuable applications in certain morbid conditions. It bears the name of sinusoidal current, and is an alternating current having certain points of resemblance to the secondary current of an induction coil. A sinusoidal alternating current is one which rises from zero to a maximum and falls away again, to be followed immediately by a reversed current which also grows to a maximum and wanes in the same manner. Each complete cycle, therefore, consists of two hemicycles or semiphases, which are equal and opposite.

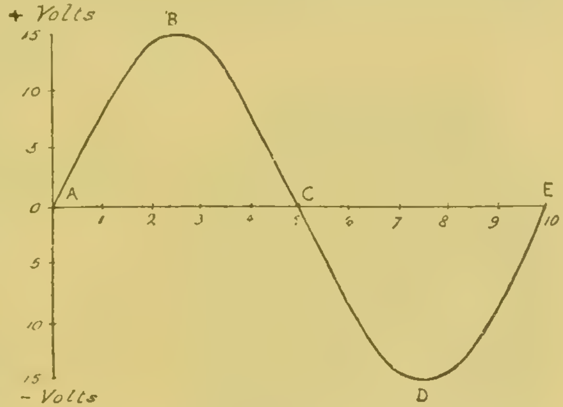


FIG. 10.—Curve of Sinusoidal Current.

The changes in value of any varying quantity, as, for example, electro-motive force or current, can be represented graphically by a curved line, just as the variations in the body temperature of a patient can be recorded upon a temperature chart. If a horizontal line be drawn to represent periods of time, and if magnitudes of electro-motive force or current be represented by distances above the base line (positive), or below the base line (negative), then an electro-motive force, gradually rising from zero to fifteen volts positive and falling again, could be represented by the curve ABC, and the continuation of the curve CDE represents a reversal of sign of the electro-motive force and a fall to fifteen volts negative, followed by a return to zero at E, the period of the whole cycle being represented by the base line ACE. Similar curves could be drawn to represent any values of a varying electro-motive force or current, and any periods of time. A curve of the kind represented is known as a simple periodic curve, or a sine curve, and the current from an alternating current dynamo is often spoken of as a sinusoidal current to signify that its wave-form approximates to a true sine curve. The current supplied by the mains of those electric supply companies whose current is an alternating one, may be used, with due precautions, as the source of the sinusoidal currents for applications to patients. The gradual rise and fall of a sinusoidal current makes it less stimulating

to the nerves and muscles than the irregular and more jerky impulses of an induction-coil current. On this account it is better borne, and larger magnitudes of current can be applied than with the coil. The frequency or periodicity of an alternating current means the number of periods or cycles occurring in one second. The periodicities of commercial alternating currents range between 40 and 100.

Polyphase Currents.—A simple alternating current, such as has been described, may be called a single-phase alternating current, to distinguish it from polyphase currents. Two-phase and three-phase currents are used for industrial purposes, and have been proposed for medical use. If a dynamo is designed with three separate sets of windings on its armature, and if these are so spaced out as to come into inductive operation in regular succession, a simple alternating current will be generated in each of the three windings in turn, and if one end of each of the three windings are joined together, and the three other ends are led out, they will convey a three-phase current to an outside circuit. For application to patients three pads or electrodes are made use of, and each in turn is positive or negative to the others in regular sequence. Dr. George Herschell has recently pointed out that three-phase currents of very low periodicity have a special action upon the abdominal viscera. It is possible that three-phase currents may in time secure a definite place in electrotherapy. It will suffice at present merely to indicate the methods.

Electrodes.—The conductors through which the current is applied to the body are called electrodes. The word electrode has also been used to describe the connexions by which the current leaves the battery or enters any instrument, and also the wire conductors of a circuit, but in medical usage the word electrode is employed to signify the special terminals which are applied to the patient. These conductors were formerly called rheophores. The variety in their nature and shape is naturally great; and it will be useful to describe some of them.

The old-fashioned brass handles and wet sponges should be wholly abandoned; the proper form of electrode to use is a disc or plate of metal covered over with chamois leather, or some such absorbent material. The electrodes must be kept clean, and care must be taken not to apply uncovered metal directly to the skin, as it produces painful effects, and may even cause sores, by electrolytic action. On this account sheaths and covers must be fitted of one or more layers of amadou, flannel, or chamois leather. These should be often renewed, and as far as possible a separate set should be kept for each patient. Absorbent cotton-wool, asbestos cloth, and blotting-paper have also been recommended for use as sheaths for electrodes.

In some medical applications both the poles of the battery are used equally, and in that case the electrodes at the two poles may be similar, but more often the current is applied to the affected part with one pole, which is then known as the "active electrode," the circuit being completed by the application of the other electrode, the "indifferent electrode,"

to any convenient part of the body; in these circumstances the active electrode generally requires a handle for its proper manipulation, while the indifferent electrode is most conveniently arranged as a simple covered metal plate, which can be applied to the surface of the body and left there during the treatment. It is generally an oval plate of pure tin or of pewter, four or five inches long. Zinc plates may also be used, and perhaps the best metal of all is silver. Thin sheet silver is not very costly. It looks clean and has the advantage that most of its compounds are insoluble and remain on the surface of the plate, where they are harmless. On one side of the plate a binding screw is affixed for the attachment of the connecting wire, and the other side is covered with a smooth piece of amadou or chamois leather, which must be moistened with warm water, or salt and water, before use. In addition there should be a sheath or pocket with a waterproof back to contain the electrode, and to protect the patient's clothes from being wetted. Red Turkey twill makes a suitable material for the front or conducting side of the sheath.

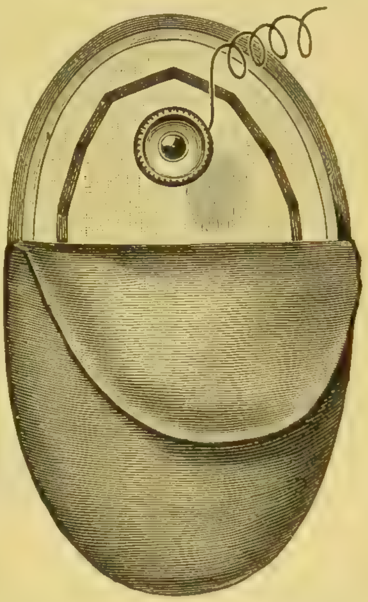


FIG. 11.—Plate Electrode and Sheath.

The indifferent electrode may be slipped between the clothing and the skin, the pressure of the clothes will then suffice to keep it in place, or if the patient is lying down, the electrode may be put underneath the shoulders or the hips, or it may be held against the chest, or the abdomen, or the back, by the patient himself, or by an attendant. In either case the operator is able to give his whole attention to the other or active electrode. Care must be taken to see that the contact of the indifferent electrode with the skin is well maintained, and that no clothing lies between. Sometimes, especially with children, it may be fastened on by a few turns of a bandage, or by a soft garter or belt of some kind. Electrodes to buckle or clasp upon a limb are figured in the catalogues, and are sometimes useful. The precaution should be taken of seeing that the proper side of the sheath and the proper face of the electrode are together, for the waterproof side of the sheath will not conduct.

Several sizes of electrode are required. Professor Erb has suggested the adoption of standard sizes, because the density of the current at the point of entry depends upon the size of the electrode, that is to say, upon the area from which the current passes to the patient. For different effects one may desire at one time a current diffused over a large surface of entry, and at another a current concentrated at a small surface. In the operation for the removal of superfluous hairs by electrolysis, the

indifferent electrode is large and the local effects on that part of the skin which it touches are imperceptible, but the active electrode is a fine needle, and the density of the current at its point is such that strong local effects are produced where it pierces the skin, even when the current is only two or three milliampères.

For practical purposes of diagnosis and treatment it will generally suffice to have three or four sizes of disc electrode, the smallest of one inch in diameter, the largest of four inches. A roller electrode and a fine wire brush are also necessary at times.

For testing purposes an electrode handle fitted with a key for closing the circuit is necessary. Electrodes with opening keys are also made, but are much less useful.

Electricity of High Potential.—*A. Statical Methods.*—These consist in the treatment of the patient, who is insulated upon a suitable stool or platform, by means of electrical charges and discharges from an electrical

FIG. 12.—Electrodes.

machine. Electro-static applications were employed in medicine almost from the time of their discovery, and early writers on medical electricity have enumerated long lists of cures effected by these means.

Static electricity deals with the properties of electrically-charged bodies, and with the phenomena of their charge and discharge. It was formerly called "frictional" electricity, because the phenomena were most readily observed with electricity at high potentials, such as could be produced by "frictional" machines. Modern static machines do not rely upon friction for the generation of their electric charges.

After the discovery of the voltaic pile the use of the electrical machine gradually fell into disuse; but it is now being revived with modern apparatus and a better knowledge of the subject. In France especially these methods have been much in vogue during the last few years, and a certain amount of scientific work has been devoted to them, so that we are beginning to gather some little trustworthy knowledge of the physiological effects of high-potential electrification. There seems to be no doubt that in this way certain general nutritive changes can be

brought about; the effect on healthy persons probably being to increase the metabolic activity of the tissues. Moreover, electro-static methods have, above all, the power of combating many hysterical manifestations, such as pains, anæsthesias, contractures, and paralyses: these last, however, depend rather upon the psychological than on the physiological effects of electricity. In comparing the so-called statical methods with other kinds of electrical treatment it is found that an important feature of the former is that very high potentials, even up to one hundred thousand volts or more, are employed. These enormous voltages can usually be applied to patients without danger, because of the small capacity of the machines used to produce them. The actual current in the discharge from a statical machine is very small. Any rise in the capacity of the apparatus is accompanied by an increase in the magnitude of the discharges, and in the sensation of shock.

The best type of electro-static machine is the Wimshurst machine; and it is advantageous to use one with eight or twelve plates, each having a diameter of thirty inches, and to enclose the whole machine in a roomy glass case to protect it from damp and from the dust which is abundantly attracted by the machine when in action.

In statical applications the patient is seated on a stool which is insulated upon a platform with glass legs, and is connected to one pole of the machine by a conductor; the electrodes, held by the operator, are connected to earth, and the second pole of the machine is also earthed. The advantage of this mode of procedure, which is rendered possible by the power of modern machines, is that the electrodes are at zero potential, which makes it unnecessary to use any device to guard the operator against shocks. The earthing of the electrodes is arranged by a long light chain connected at one end to a gas or water pipe in the building. The electrodes have the form of single or multiple metallic points, or knobs, or rollers. Leyden-jar discharges are now seldom used.

As soon as the patient becomes charged he feels certain sensations. The hair begins to move, and on the scalp and face, and to a less degree on other parts, he feels as if lightly touched by gossamer or cobwebs. The effect of a static charging is to increase the frequency of the pulse and its regularity. The blood pressure is raised, the action of the skin is increased, and nutritive exchanges are accelerated. The effect on the nervous system is sedative, patients sleep better, and they may even show a tendency to fall asleep during the process of treatment.

If when the patient is charged on the platform a point electrode is presented to him, he feels the sensation of a wind blowing towards him from the point; this is the electric breeze, or brush discharge. It can be felt when the point is a yard away, but becomes much more strongly felt when the point is brought nearer. The breeze, which is felt as a cool wind upon the bare skin, acquires a pricking hot character when directed upon covered parts, and the prickly sensation is greater when the patient is positively charged. Usually, therefore, the patient is charged positively, except when the mildest form of breeze is desired,

as may be the case with timid or unaccustomed patients. The breeze produces a very grateful sensation when applied to the scalp, and to the nape of the neck, and it is usual to arrange a special electrode for this head breeze by means of a hinged arm supporting a wire crown or tassel, at a certain distance above the patient's head. The breeze is called the "negative breeze" when the patient is positively charged, and *vice versa.* The breeze can be varied in strength by varying the distance between the point and the patient's surface. It is more agreeable if the electrode is kept in movement. The effect of a strong negative breeze upon the spinal region and the back is very invigorating, and leaves a warm glow.

In practice it is found that some patients experience a marked feeling of improvement as soon as the charging begins, while others remain indifferent, or may even show by their words or movements that they find it uncomfortable. It is probable that this is due to the effect on blood pressure. Those whose pressure is low feel better as soon as it is raised, while those whose blood pressure is already high are made uncomfortable by the treatment.

The good effect of breeze discharges upon pain in the superficial cutaneous nerves, as for example in the headaches of fatigue or debility, and in neuralgia, is prompt and striking.

Statical applications undoubtedly act upon the function of menstruation. In patients receiving a course of treatment for conditions quite unconnected with the generative functions it is common to remark some effect upon the menstrual periods. Professor Doumer, of Lille, has published his notes on 400 women treated by static electricity. Among these cases there were 178 who had some pains or discomfort about the date of the commencement of their periods, and 130 of these were relieved of these symptoms, while the remainder were not. Menstrual irregularity was present in 51 cases and quickly disappeared in 31. These results followed for the most part upon simple electro-static charging, but the discharge of the point electrode applied to the lumbar region seemed to increase the effect.

Among the observations on statical treatment which have recently excited fresh interest are some which seem to show that the brush discharge of the statical machine has a curative effect upon cutaneous affections of very various kinds. Thus it has been successfully used in pruritus, which is so often intractable to many forms of treatment, in psoriasis, in eczema, and in varicose ulcers of the leg. Even lupus and rodent ulcers are benefited by the brush discharges of the static machine, though the effect is feebler than that produced by high-frequency discharges, which are somewhat similar and more powerful.

B. High-Frequency Currents.—When a charged conductor is discharged, it happens under certain conditions of the discharging circuit that the discharge is an oscillatory one. The oscillations die away very quickly, but while present they may have a periodicity of hundreds of thousands, or of millions, a second. The rate or frequency of oscillation is determined by the nature of the circuit. With small capacities and

with small self-inductions, the rate of oscillation is more rapid than with large values of either of these components.

To illustrate the phenomena by analogy the behaviour of water in an hydraulic apparatus is commonly employed. Imagine two open jars of water connected by a pipe in which is a tap. When the tap is open the jars are placed in communication so that water can flow from one to the other. With the two jars standing at the same level and the tap closed, one jar is filled with water and the other is left empty. This illustrates the charging of the condenser. The tap is then opened suddenly and the water flows through the pipe, until finally a state of equilibrium is reached, with the water standing at the same level in both jars. This represents the discharge of the condenser. If the pipe of communication is narrow, there is resistance to the free passage of the water, and the flow is a continuous gradual one. If the pipe is a wide one the water flows rapidly and only reaches the same level in the two vessels after a series of oscillations, in which the height of the water-level is alternately greater in the first and in the second of the jars.

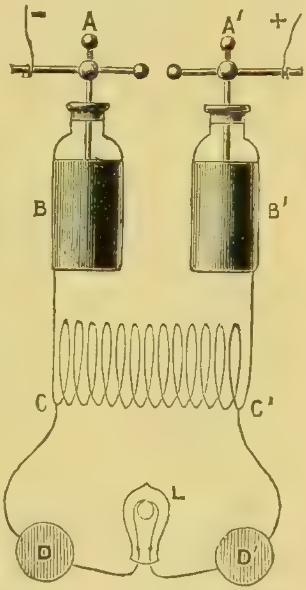


Fig. 13.—Plan of apparatus for oscillatory discharges. The Leyden jars B B′ are charged from the two poles of an electrical apparatus, and discharge between the knobs at A A′. C C′ is a solenoid or helix, connecting the outer coatings of the jars.

So again the discharge of a condenser may be compared to the movement of a spring which has been bent and is let go. If free and unobstructed it comes to rest only after a series of oscillations or vibrations. It comes to rest without oscillations if its movement is opposed by friction. In the case of the electrical oscillation friction is represented by the ohmic resistance of the circuit. The oscillatory discharge of a Leyden jar is the basis of high-frequency current treatment; it has been studied by Elihu Thomson, Nikola Tesla, and D'Arsonval, and the last-named physicist has specially studied these "high-frequency" phenomena in their relations to physiology and medicine. Some remarkable results have been obtained. The apparatus required is comparatively simple; the principle is to charge Leyden jars whose outer coatings are connected by a helix of wire, or solenoid, as in Fig. 13. The inner coatings of the jars terminate in knobs, whose distance apart can be adjusted to suit the sparking distance of the charging electromotive force. The jars can be charged from a Wimshurst machine, or from an induction coil of large size, or from a high-potential transformer working from the alternate-current supply mains. The output is least in the first method.

The jars, when charged to a sufficient potential, discharge in an oscillatory manner across the air-gap and through the solenoid connecting

the outer coatings, and the latter become the seat of electro-magnetic induction effects, comparable to those of the primary circuit of an induction coil, so that a derived circuit formed by wires leading from the two ends of the coil give energetic discharges. In fact, the apparatus may be regarded as a modified induction coil, the exciting current being supplied from the discharge of the jars instead of from a voltaic cell, while the spark-gap takes the place of the contact-breaker. Owing to the suddenness of the discharge the changes in the magnetic field of the circuit are very rapid, and very powerful induction effects are set up both in the solenoid itself by self-induction, and round it by mutual induction, and a secondary coil wound over the solenoid also gives very conspicuous effects. The figure (13) shows an arrangement, due to D'Arsonval, for demonstrating with high-frequency currents. D D′ represents two persons holding between them an incandescent lamp L, and having their other hands connected to the terminal points of the solenoid; under these conditions the current between C and C′ traverses the lamp and the arms of the two experimenters, and though the current is sufficient to make the lamp glow brightly they feel no shock.

The solenoid is usually made of about twenty turns of thick copper wire.

The methods of applying high-frequency discharges can be arranged in two main divisions. In the one the apparatus is made use of to generate brush discharges, and these are brought to bear upon the surface of the patient by means of suitable electrodes. These may take the form of bare metallic points, or there may be an arrangement of a dielectric such as an exhausted glass tube, or a tube filled with salt solution with an internal metal connexion. In the latter arrangements the alternate charging and discharging of the inside of the glass is accompanied by an equal and opposite charging and discharging at its outer coating, and this shows itself as a violet flow or brush discharge passing between the outer surface of the glass and the patient's skin. If the potentials at the extremities of the solenoid connecting the outer coatings of the Leyden jars are insufficient to give brush discharges of sufficient power they can be increased by the use of a device known as a resonator, or by an arrangement of primary and secondary coils. Brush discharges of great length and volume can be obtained in this way, and there is no room for doubt as to the good effects produced by these brush discharges in many forms of disease affecting the surface of the body. Chronic eczema, psoriasis, acne, pruritus, many forms of indolent ulcer, tuberculous affections of the skin (lupus), and rodent ulcer, can be much benefited by their employment.

In the other division of high-frequency therapeutics the currents of the solenoid are caused to traverse the patient directly. Several arrangements are in use. In the simplest, the electrodes leading to the patient are connected to the ends of the solenoid which joins the outer coatings of the Leyden jars, and are applied to the body so as to include a particular limb or region. The patient is therefore in electrical connexion

to the ends of the solenoid; or, again, the patient is connected to one end of the solenoid while the other is led to a large sheet of metal insulated and placed beneath his chair or couch, and by reason of the augmentation of his capacity produced in this way currents of large magnitude can be set in motion, surging to and fro between the patient and solenoid. Readings of current up to several hundred milliampères are not uncommonly obtained. This method is spoken of as treatment by auto-condensation or by the condenser couch. Finally, the solenoid connecting the Leyden jars may be made so large that the patient can be enclosed in it, and his body is then the seat of eddy currents, a method known as "auto-conduction."

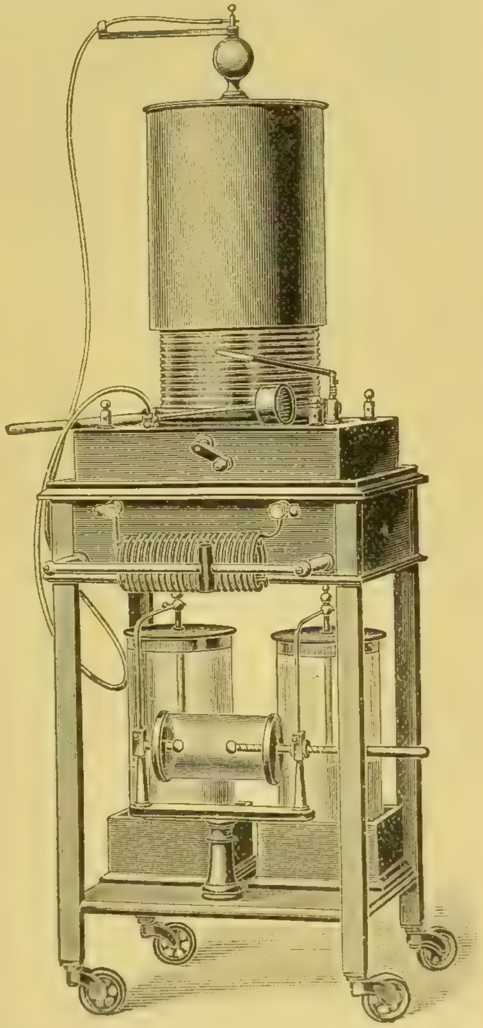


Fig. 14.—High-frequency apparatus with resonator.

These modes of application differ from those in which the brush discharge is employed. It has been claimed that the large currents which are set in motion by them are able to exercise a powerful influence upon the nutrition of the body and to arrest various morbid processes. It is not yet established beyond doubt that such applications have any great value. That there is an influence upon nutrition is undoubted, as has been fully proved by D'Arsonval's physiological experiments; but although a vast mount of work has been done in recent years with high-frequency, there is still much to learn concerning its action upon disease. It is interesting to note that whereas statical applications raise the blood pressure, the effect of high-frequency applications is to lower it. A most instructive paper on this point, with many illustrative cases, has recently been published by Moutier. The cases were old people with definite signs of arteriosclerosis. The reduction of pressure produced by applications of high-frequency showed considerable permanence.

The Reactions of Motor Nerves and Muscles.—The nature of the responses seen when a motor nerve or a muscle are stimulated by the

battery current and the induction coil are among the facts of elementary physiological teaching, and have been made the basis of the testing of the condition of the nerves in disease. In health the battery current produces a single twitch of a muscle when the circuit is closed, and also when it is opened. In the interval between closure and opening the muscle remains quiescent although the current is still flowing. The magnitude of the current necessary to cause a minimal contraction when the negative electrode is favourably placed over a superficial nerve-trunk is about one milliampère. With the positive pole a current of about twice this strength is needed, and in both cases the contractions are more readily produced at the closure than at the opening of the circuit. Thus there are four possible ways of producing a contraction :—

1. Closure of circuit with kathode on the nerve or muscle, or kathodal closure contraction = KCC.
2. Closure with the anode on the nerve or muscle, or anodal closing contraction = ACC.
3. Opening with the anode on the nerve or muscle, or anodal opening contraction = AOC.
4. Opening with the kathode on the nerve or muscle, or kathodal opening contraction = KOC.

These are arranged in the order of their appearance in health. When stronger currents are used the muscle is not fully relaxed during the steady passage of the current between the times of closure and opening, but is in a state of partial contraction, which is known as *duration tetanus.*

The effect of the induction-coil current, or of any rapidly varying current, is to throw the muscle into a state of contraction or tetanus, which persists during the whole time of the passage of the current. The induction-coil current acts as a rapid succession of separate stimuli.

Electrical stimuli applied directly over the body of a muscle act through the intermediary of its motor-fibres, which are able to convey the impulse more rapidly than the muscle-fibres can convey it, but the muscle can also contract independently of its motor-fibres, as is proved by its behaviour when under the influence of curari. The superficial muscles have a motor-point, or point most favourable for their stimulation, to which the electrode should be applied when testing.

Test for Death.—Among all the suggestions which have been made for determining with certainty the death of an individual there are none which compare in certainty with the electrical testing of the muscles. Their contractility only persists for a short time after death, and then disappears gradually. If the muscles of a person supposed to be dead cannot be made to contract to electrical stimuli life may be considered extinct. Onimus and Legros have shown that there is a stage in the dying of a muscle at which it shows the reaction of degeneration. This change sets in about four hours after death. Marie and Cluzet found

PLATE I.

Motor Points.

PLATE II.

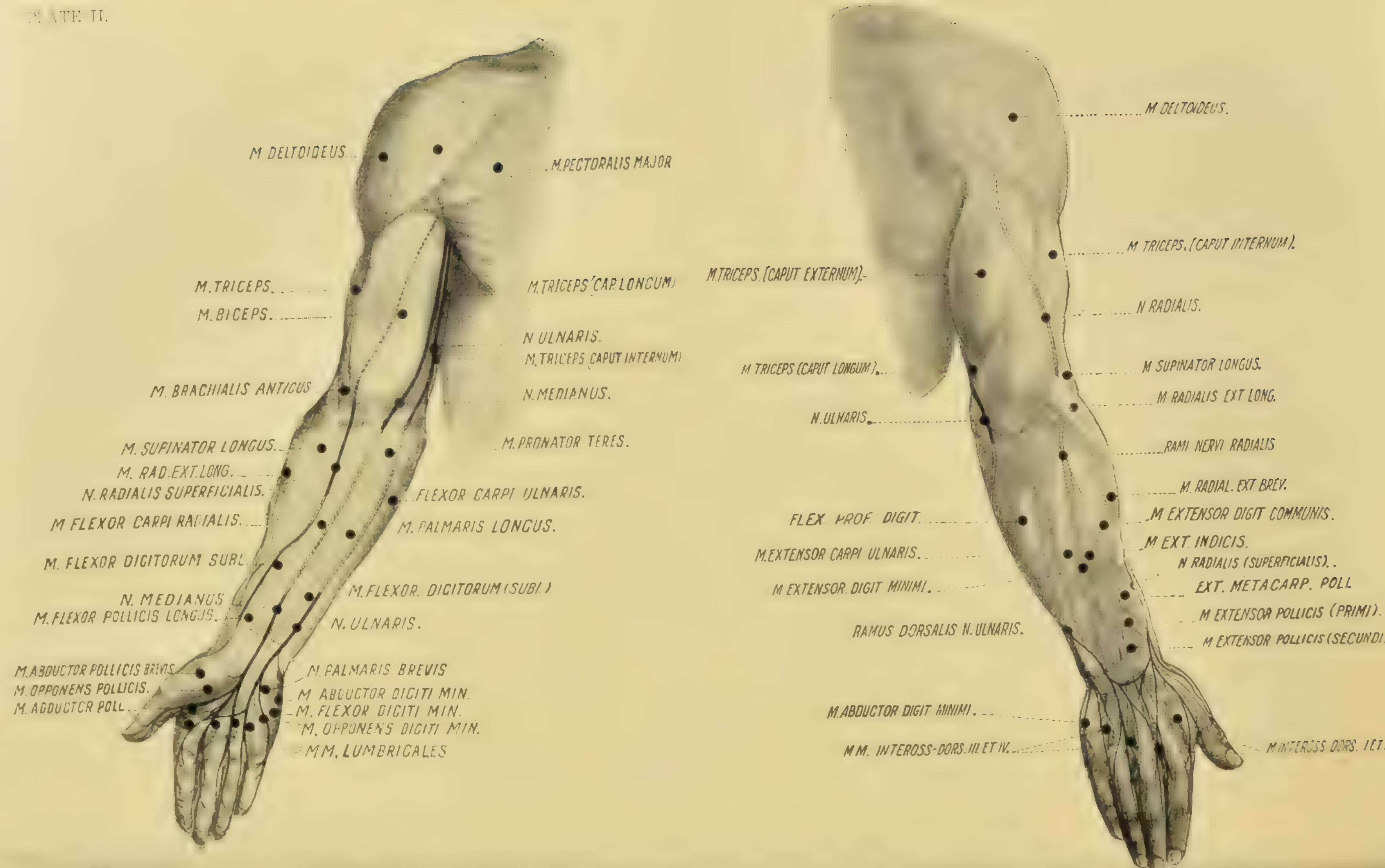
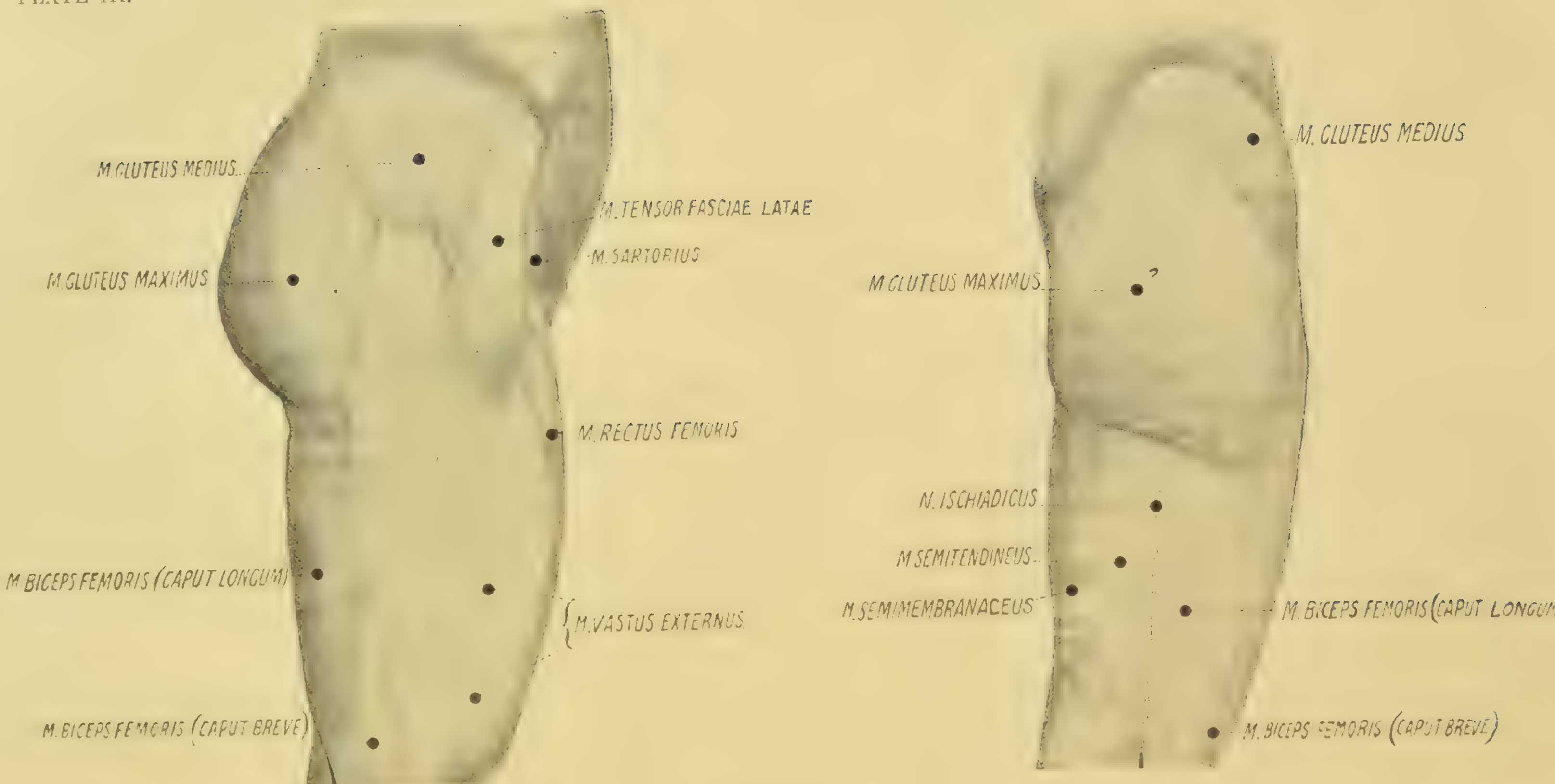

M DELTOIDEUS
M.PECTORALIS MAJOR
M.TRICEPS.
M.BICEPS.
M.TRICEPS (CAP. LONGUM)
N ULNARIS.
M.TRICEPS CAPUT INTERNUM)
M. BRACHIALIS ANTICUS
N.MEDIANUS.
M. SUPINATOR LONGUS.
M. PRONATOR TERES.
M. RAD. EXT. LONG.
N. RADIALIS SUPERFICIALIS.
FLEXOR CARPI ULNARIS.
M FLEXOR CARPI RADIALIS.
M. PALMARIS LONGUS.
M. FLEXOR DIGITORUM SUBL.
N. MEDIANUS
M. FLEXOR. DIGITORUM (SUBL.)
M. FLEXOR POLLICIS LONGUS.
N. ULNARIS.
M. ABDUCTOR POLLICIS BREVIS
M. OPPONENS POLLICIS.
M. ADDUCTOR POLL.
M. PALMARIS BREVIS
M ABDUCTOR DIGITI MIN.
M. FLEXOR DIGITI MIN.
M. OPPONENS DIGITI MIN.
MM. LUMBRICALES
M DELTOIDEUS.
M TRICEPS. (CAPUT INTERNUM).
M TRICEPS. (CAPUT EXTERNUM)
N RADIALIS.
M TRICEPS (CAPUT LONGUM)
M SUPINATOR LONGUS.
M RADIALIS EXT LONG.
N. ULNARIS
RAMI NERVI RADIALIS
M. RADIAL. EXT BREV.
FLEX. PROF. DIGIT.
M EXTENSOR DIGIT COMMUNIS.
M EXT INDICIS.
M. EXTENSOR CARPI ULNARIS.
N RADIALIS (SUPERFICIALIS).
M EXTENSOR. DIGIT MINIMI.
EXT. METACARP. POLL
M EXTENSOR POLLICIS (PRIMI).
RAMUS DORSALIS N. ULNARIS.
M EXTENSOR POLLICIS (SECUNDI)
M. ABDUCTOR DIGIT MINIMI.
MM. INTEROSS-DORS. III. ET IV.
M INTEROSS DORS. I ET II

PLATE III.



Motor Points.

PLATE IV.

Motor Points.

that the muscular irritability disappears more or less quickly according to the nature of the disease causing death, but that the reactions begin to change after half an hour has elapsed, and that a complete reaction of degeneration begins to make its appearance in about one hour.

The Motor-Points.—These are the points to which the testing electrode should be applied in order to set up a contraction most easily in the subjacent muscle, or they are points at which motor nerve-trunks can be easily reached. They represent positions at which a maximum effect can be produced by a given current, and a good knowledge of the motor-points enables one to carry out a test with comparatively weak currents, and therefore with the least amount of discomfort to the patient. Many diagrams of the motor-points have been prepared, most of them being based upon von Ziemssen's plates.

Von Ziemssen prepared his plates by exploring the surface with a testing electrode, and marking the points as they were found. He found by dissections on the dead body that the excitable points corresponded to points at which the main nerve supply entered the muscle.

In recent years the distribution of the motor-points has been mapped out afresh by several independent observers. The plates of the motor-points which illustrate this article are taken from the admirable life-size drawings of Dr. Schatzsky, of St. Petersburg.

It should be borne in mind that the motor-points are not quite constant for different individuals, their exact place varying a little in different cases, but not so greatly as to diminish the value of knowing their positions. In actual practice the best position of the electrode can be readily found by experiment, by moving it about in the neighbourhood of the usual position of the motor-point of any particular muscle until the contraction shows that the exact spot has been touched. The ease with which the motor-points can be found depends a great deal upon the amount of subcutaneous fat present, and the examination of the deeper muscles is much more difficult than of the superficial layer; indeed, in the case of some of the deep muscles it is almost impossible to produce satisfactory evidence of a contraction limited to the muscle sought, for the diffusion of the current will throw into action the neighbouring superficial muscles and so obscure the result. It is very important to place the patient's limb in a good position, so that any muscular movement looked for may be readily seen; the muscles must be lax, the limb should be supported by the hand of the operator, or should rest easily upon the table or couch. A finger lightly placed over the tendon of the muscle tested will often feel a movement there before it can be seen in the body of the muscle. Testing should be done expeditiously. It is well always to try the strength of the current on one's self before touching the patient.

It is assumed that the action of the individual muscles is known, so that when a contraction is produced it can be referred to its proper muscle.

In certain forms of paralysis the reactions remain unchanged, and in

others they undergo a profound and characteristic alteration, of the which the following are the important features:—(1) There is no response in the muscle to any stimuli applied to the motor nerve. (2) There is no response to interrupted currents even when the electrode is applied directly over the muscle. (3) The battery current when applied directly to the muscle produces a contraction of a very peculiar character, which can easily be distinguished by the eye from the contraction in a healthy muscle, because it is a slow and sluggish movement, and not a rapid twitch. These slow and sluggish contractions may be produced by smaller currents than those necessary in health, or they may only appear with large currents. The irritability of the muscle is said to be increased or decreased accordingly, but the feature of prime importance is not the increase or decrease of irritability to the battery current, but the change in its character from quickness to sluggishness. The loss of irritability to interrupted currents, both in the muscle and the nerve, is the other important feature.

This change, or group of changes, in the behaviour of the nerve and muscle is known as the *reaction of degeneration*, and its value consists in the fact that it is associated with injury or disease of some part of the lower neuron. Its recognition in a case therefore implies that the cause must be sought for in that tract. The term reaction of degeneration was introduced by Erb, and to his careful study of the peculiar group of changes which constitute the reaction we owe the most important truth connected with the use of electricity in diagnosis. Its discovery arose from an observation of Baierlacher in 1859 that the muscles in a case of facial paralysis did not respond to the current of an induction coil, but reacted with unusual readiness to the battery current.

Erb, in his account of the reaction of degeneration, lays stress upon the presence of an inversion of the normal polar effects in cases showing it. A recollection of this opinion of Erb's still survives, and is very widely accepted, but though the anodal closing contraction may be greater than the kathodal closing contraction in some cases of the reaction of degeneration, it is by no means constantly observed, and therefore has no diagnostic value. Probably the inversion of formula sometimes observed is an accidental effect, depending upon the relative positions of the two electrodes, and upon the position of the electrode in relation to the motor-point.

In testing muscles which are suspected of showing a reaction of degeneration it is useful to observe the effect produced with the testing electrode on the distal end of the muscle instead of on the motor-point. In health the effect of the current in causing contraction is greatly reduced when the electrode is so placed, but in many cases of the reaction of degeneration a better contraction is obtained with the electrode on the distal tendon. Its significance is that the nerve is degenerated, and that the motor-point has, therefore, lost its value, and that to stimulate the muscle most effectively the current should be made to traverse its whole length.

The reaction of degeneration is the most important reaction of disease in nerves. Other alterations from the normal may commonly be observed, but their diagnostic significance is less. It will suffice to enumerate them. Thus simple increase of irritability and simple decrease of irritability may be observed either to the coil current or to the battery current. When these conditions appear to be present it is useful to verify the state of the patient's resistance and the magnitude of the current in the circuit, for a high resistance might simulate decreased irritability, and *vice versa.* Occasionally cases are met with which show the sluggish contraction to the battery, which is characteristic of the reaction of degeneration, and yet have preserved some of their contractility to the induction-coil current. These cases are said to show a *partial reaction of degeneration.* Its significance is very much the same as that of the complete reaction.

Other abnormal conditions consist in the too-ready production of duration tetanus; the *myasthenic reaction*, in which symptoms of fatigue in the muscle appear very quickly during the testing, and the *myotonic reaction*, which is a condition of slow relaxation of the muscle-fibres after they have been made to contract. Special works on electro-therapeutics should be consulted for further details on these matters.

Practical Testing.—In general, it is best to test the muscles singly by the application of the testing electrode to the motor-points. It is less often useful to test them in groups through the motor nerve-trunk. Care expended in moistening the skin and the electrode beforehand makes the process easier of performance and less painful. A little salt in the water helps matters, although it is often omitted, as it tends to corrode the electrodes. The water should be hot enough to make the electrodes feel comfortably warm.

The induction coil should be used first, and then the battery to verify the opinions formed from the coil-current test. If the battery test is omitted cases with the partial reaction of degeneration may be overlooked and regarded as normal. In testing with the battery the results should be checked by the galvanometer, and in all testing in which it is feasible comparisons between the side tested and the corresponding sound limb should be made. It is well to practise upon one's own muscles, and the exact position of the motor-points of the muscles of the limbs should be learnt by heart. For the muscles of the face weak currents are sufficient, since currents strong enough for testing the muscles of the limbs are felt painfully on the face. The upper limb muscles react more easily than those of the lower. Sensibility can be tested by means of induction-coil currents, but they are not of any special advantage for the testing of sensation.

Methods of Electrical Treatment.—In the application of electricity to medical treatment certain methods must be followed in order to obtain the effects desired. The form of current to be employed, and the proper strength of current and the duration of the applications must also be considered. A large part of the benefits derived from electrical applications can be ranged under the heading of stimulation, and by virtue of the

stimulating effect which is produced by a general application of electricity to the whole body one is enabled to obtain good results in the treatment of many general morbid conditions.

Electrical treatment has long been dominated by the idea that its chief utility lay in the treatment of nervous disorders, and that local applications to paralysed parts formed the only kind of electrical treatment worth following. This is by no means the case, and of late years the advantages of general electrisation of the whole body for general disorders has received more attention. The effect of electrical applications to the body as a whole in improving nutrition are now fully established. The influence exercised by general electrisation in states of defective nutrition may be presumed to include two separate factors, the one a stimulation of the nutritive processes, and the other, which may be equally important, being a stimulation of processes of elimination. General electrisation is used as a stimulating method of treatment in states of debility or defective nutrition, for instance, during tardy convalescence after exhausting illness, in anæmic people, in neurasthenia, in rickets and in rheumatoid arthritis. After influenza its employment is often productive of rapid improvement, and diphtheritic paralysis also responds very satisfactorily to treatment by some form of general electrisation.

The Electric Bath.—The best mode of applying general electrisation is by the medium of an electric bath with the sinusoidal current, or failing that, with induction-coil currents. An earthenware or wooden bath-tub is used, and it is fitted with large metal electrodes at the head and foot. A third movable electrode, in the form of a paddle, is attached by a wire to the foot-plate, and is applied by being moved about in the water so as to concentrate the current upon any desired part. The water in the bath should have a temperature of 99° Fahr.

A considerable proportion of the current traversing the bath passes by the water without entering the patient, but a fraction varying between one-eighth and one-tenth actually passes through the tissues of the patient.

Other Methods of General Electrisation.—It is also possible to give general treatment in other ways, as by electro-static charging or by applications of high-frequency currents. Under the titles of "general faradisation" and of "central galvanisation" procedures have been described which may conveniently be considered under the general heading of general electrisation. The former of these consists in applying induction-coil currents to the general surface of the body of the patient. One electrode is placed in a foot-bath in which the feet are immersed, while the other is systematically applied to the different areas of the body, and particularly to the back, neck, arms, and legs. Where an electric bath can be provided general faradisation of this kind will be rendered unnecessary, as the desired treatment can be carried out more efficiently by the bath method, with the additional advantage that the hot water in the bath serves to keep the patient warm and comfortable during the time of the application.

Central galvanisation consists in the application of battery currents to the region of the neck and spine, so as to influence the nerve centres.

Drs. Beard and Rockwell, who introduced the method, advise that the negative pole should be held to the epigastric region while the positive is applied to forehead and temples, to the neck over the vertebræ, and along the whole length of the vertebral column. A current of five or ten milliampères should be used, except for the head, where its magnitude should be reduced.

In connexion with this procedure, it is of interest to note that Capriati has shown from experiments on healthy individuals that the application of currents of ten or fifteen milliampères to the spine for ten minutes produces a marked effect upon the muscular power, as tested by the ergograph.

The Choice of Current.—The effects of electrical applications of different kinds upon nutrition have been examined by D'Arsonval, who has made the following comparisons of the effects noted by him. Under the influence of (1) electro-static treatment there is a slight increase of respiratory exchanges. This is not due to the presence of ozone, as has been suggested, for it is not noticed if the subject is merely placed in the neighbourhood of a static machine in action without being electrically connected with it.

(2) The continuous current, in spite of the general belief in its trophic effects, has given negative results both in experiments upon animals and upon human beings, so far as an effect upon the respiratory exchanges is concerned, although it may have other special influences upon cellular activity. (This refers only to steady unvarying battery currents.)

(3) Induction - coil currents, by producing more or less extensive muscular contraction, augment the oxidation processes of the body. By severe tetanisation of all the muscles of the body the temperature of an animal may be so raised as to lead to its death from this cause. Induction-coil currents, even when so gentle as to cause no muscular contractions, can nevertheless cause modifications in the nutritive exchanges of the body, with increased production of heat.

(4) The sinusoidal current gives very marked effects. By its use the respiratory exchanges can be augmented by 25 per cent without provoking any muscular contractions whatever. This result is obtained both in animals and in human beings.

(5) The effects of high-frequency currents upon the respiratory exchanges of the body are very marked. The elimination of CO_2 in the case of a human being subjected to this form of application has been observed to be increased from 17 to 37 litres per hour. Associated with this there is a considerable increase in the production of heat, namely, from 79 calories to 127 calories per hour, the body temperature remaining steady at the normal point.

Debedat has studied the effect of different forms of electrical applications upon the growth of muscle. His experiments were made on the muscles of young rabbits with various forms of current. The group of hamstring muscles was chosen; those of the left side were stimulated in various ways daily during twenty days, for four minutes a day; those of

the right side were left untreated for purposes of comparison. At the end of the period the animals were killed, and the muscles of the two sides were carefully removed and weighed; portions were also hardened and examined microscopically. The results showed a gain of 40 per cent in weight on the stimulated side from the rhythmic induction shocks, and of 18 per cent from the rhythmic battery current. The prolonged tetanisation caused a marked loss of weight; the prolonged steady battery current a slight increase in weight. Adhesions had formed between the skin and the muscle, at the points of application of the electrodes in the last case. The gain in weight was due to a true growth of the muscle; the loss was accompanied by histological evidence of damage to the muscle-fibres. Static sparks produced no effect. The author concludes that the most advantageous mode of promoting the growth of muscle by electricity is to use an induction coil, and to arrange the periods of contraction and repose of the muscle, so as to approximate to the conditions of a muscle during the performance of rhythmic gymnastic movements—namely, about thirty periods of contraction and thirty of rest per minute, prolonged tetanisation being distinctly harmful.

Thus it is apparent that a large proportion of the cases which are to be treated by electricity will require varying currents rather than steady currents, but we must bear in mind that this does not necessarily mean that the induction coil is to be used in the majority of cases. The battery current can also be made to vary, as has already been shown, and in many instances the slow variations which can be produced with the battery current will be preferred in treatment. Induction-coil currents, from their rapid and abrupt variations, may be too stimulating, and may affect the cutaneous sensory nerves too much, and this may prevent the use of currents of sufficient magnitude for influencing the deeper parts. Or they may be unsuitable in other ways, as, for instance, for influencing unstriped muscle when vasomotor effects are desired or when the intestine or the bladder are to be treated.

The induction coil will be chosen for the treatment of paralysed muscles if they are in a condition to respond to it. If they show the reaction of degeneration and have lost the power of responding to induction-coil currents, then the battery current, to which the muscle can still react, may be chosen in preference, or, as it is probable that the effects of the two methods do not coincide, it seems more reasonable to advise treatment by both, and to treat paralysed muscles by means of applications of current from the battery as well as from the induction coil when they show the reaction of degeneration.

The opinion is often expressed that the induction-coil current is useless in the treatment of such forms of paralysis, but with this the writer does not agree. The results obtained by Duchenne in the treatment of various forms of paralysis by induction-coil currents are a sufficient testimony to their value in many forms of paralysis which show a reaction of degeneration.

It is true that a muscle showing the reaction of degeneration will

contract to the battery current only, and in so far as the contraction of a muscle is a good thing for the muscle, the battery current may be better than that of the induction coil, but it does not follow that the amount of benefit produced by the application can be measured by the amount of visible contraction set up.

It is often said that electrical applications are useful in cases of paralysis, because they serve to maintain the nutrition of the muscles until the nerve has time to recover its functions. This does not express matters quite correctly.

A muscle whose motor nerve has been seriously injured will degenerate and waste quite irrespective of being made to contract by electrical applications. If the nerve has been severed the electricity can only be of service after reunion has been effected. In less severe injuries and in disease the action of the electricity is exerted not only upon the muscle, but also upon the injured nerve. It serves to stimulate the natural tendencies to repair, it influences the circulation through the parts which are injured and are paralysed, and by its effect on the contractility of the muscle tends to promote its growth during the period of natural recovery, and to shorten the time required for this process, but it will not prevent those changes in the muscles which naturally follow severe injury or disease of the nerve nucleus or of the motor nerve-trunk. Thus in paralytic cases the value of electrical applications lies in their power of stimulating the activity of the natural processes of repair. If the battery current is used the stimulating influence is chiefly felt when the current is made to vary in some way by interruptions and closures of the circuit, or by the movements of the electrode over the surface, while with the induction coil the variations are automatically produced in the apparatus.

For the relief of painful affections the continuous current is the best. It is true that some neuralgic pains may be relieved by induction-coil currents, acting as a counter-irritant by means of their painful effect upon the skin of the affected part, but in general it is found that the pains of neuritis and other painful conditions are unfavourably influenced by rapidly varying currents. When the battery is used for the relief of pain it is best to avoid sudden changes in the current, and to treat it either by means of a steady flow of current through the painful part, or with gentle, slow variations of current. Large electrodes should be used and large currents administered.

The introduction of drugs into the painful area by the electrolytic effect of the current upon the migration of ions has been recommended recently. Quinine and salicylic acid ions have been found useful. The former drug introduced electrically has even been successful in cases of typical severe trigeminal neuralgia. The quinine, in the form of hydrochloride dissolved in distilled water, is used to moisten the coverings of the anode, and this is applied to the affected region. When drugs are to be introduced the coverings of the pad should consist of about a dozen layers of lint, well saturated with the solution.

Most localised electrical treatment is applied by the use of an indifferent

and an active electrode, as already described. The size of the active electrode must be suited to the part to be treated, and even more so to the magnitude of current which is to be used. Those commonly used are nearly always too small. Except for the localisation of current in small areas, the surface of the electrode should be at least two and a half inches in diameter, while a four-inch size is better for many applications to the trunk and limbs. The indifferent electrode should be larger still, because its position is stationary during the application, and the products of electrolysis are concentrated in one place, and may produce burning sensations, which will necessitate the reduction of the strength of current. The electrodes must be well soaked in warm water before use, and the addition of a little salt to the water improves matters by reducing the amount of resistance of the skin. The region to be treated also requires a preliminary moistening with warm water or salt solution. The greater the care taken in the preliminary moistening of the skin and the electrodes the greater will be the comfort of the patient.

The active electrode may either be held still (stabile) in one spot during the application, or it may be slowly moved over the affected area, when the application is called "labile." If closures and interruptions of current are used they can be made by the employment of a handle with a key for the purpose, or, failing this, the commutator of the battery can be used. When very large currents are to be used (stabile) for a length of time large electrodes moulded to the part are useful. In the treatment of trigeminal neuralgia such large electrodes have been used with advantage.

A bath of water sometimes forms a convenient electrode, especially as a foot-bath or arm-bath, the circuit being completed by means of a pad affixed to some part of the body. Arm-baths and foot-baths are often very useful in electrical treatment, both in the form of monopolar and of bipolar baths. The monopolar bath is a vessel of water with one electrode immersed in it the circuit being completed by a pad, as already described. The bipolar bath resembles the ordinary full-length bath in miniature, and has an electrode at each end, the current passing from one to the other, and traversing the water and any limb or part which may be immersed in it. By using two vessels of water with one electrode in each, and immersing an extremity in each, the arrangement becomes one of two monopolar baths, and in this way current can be passed from hand to hand, or from foot to foot through a patient. This arrangement is often useful, and is particularly so when electrolysis is used as a means of introducing a drug or of eliminating some toxic substance. Lithium has been introduced in this way by adding lithium salts to the water in the bath containing the positive pole. The four-cell bath of Dr. Schnee is an elaboration of this method. It consists of a chair fitted with four baths, each containing an electrode, and by suitably adjusting the connecting wires the current can be caused to traverse any two or more limbs as required.

These arm-bath and foot-bath methods are very often useful in cases of paralysis of the muscles of the forearms and hands, as, for example, in

the extensor paralysis of lead poisoning, and in paralysis from pressure or other injuries of the nerves of the forearm; also in rheumatic and gouty affections of the hands, Raynaud's disease, and in chilblains. A consideration of this list will show how often these local baths can be of service, particularly in general practice or in the electrical department of a hospital. Moreover, the bath method greatly simplifies electrical applications by dispensing with the tedious process of rubbing the electrodes over the affected parts. The constant current, the induction coil, or the sinusoidal current can all be applied by means of baths. An oblong stoneware trough, such as is made for kitchen use, can easily be adapted for these baths, and a good form of electrode to use in them consists of a piece of sheet metal, cut in a battledore shape, with the handle bent over in the form of a hook, by which the electrode can hang from the end of the bath. A binding screw is soldered to it for the attachment of the wires. Suitable vessels for arm-baths are also made of wood-pulp.

Rhythmic Interrupters.—In many forms of electrical application it is of advantage to be able to vary the flow of current in a rhythmic manner. The experiments of Debedat (p. 459) have established this, and clinical experience supports it. Several mechanical devices have been invented for the purpose of gradually turning the current on and off, and among these one may be mentioned which has stood the test of several years' constant use in the electrical department of St. Bartholomew's Hospital. It is an application by Leduc of the metronome which has long been used in physiological work for making and breaking circuits at a slow rate. The modification proposed by Leduc has the effect of causing the current to wax and to wane in a gradual manner, which is generally superior to abrupt makes and breaks of circuit. It is arranged by fixing a slender curved wire of aluminium to the moving rod of the metronome, and as this swings to and fro the rod gradually dips down into a vessel of water, and out again. At the bottom of the vessel is a conductor by which the circuit is completed. As the moving rod approaches the bottom of the vessel the resistance of the circuit gradually lessens, and the current increases in magnitude, decreasing again as the moving wire recedes again when the metronome swings in the opposite direction.

The Choice of Pole.—With battery currents the differences between the effects produced at the two poles are well marked. The greater ease with which the kathode causes muscular contraction has determined the choice of that pole in the treatment of muscular weakness and paralysis, while the sedative effect of the anode, as observed in the physiological phenomena of anelectrotonus, would indicate the superiority of the anode in painful affections. The rule laid down by Remak for the direction of the flow of current was that the current should pass along the nerve-fibres in the direction in which they conduct, namely, downwards to the periphery in the treatment of motor affections and upwards from the periphery for sensory disorders. With the induction coil the influence of pole is less important. If the "extra current" of the primary is used there is a positive and a negative pole, but with the secondary the current

is alternating, and the predominance of the effect of one wave over the other does not appear to be important enough to require much consideration.

Magnitude of Current.—With battery currents, the galvanometer provides the means of regulating the dosage. For most forms of local treatment, a current ranging between five and ten milliampères is an average quantity, and may be too much for children, or for sensitive or nervous people, at the commencement of treatment; the current must not be switched on or off abruptly, but gradually, the patient being carefully watched for any signs of pain or discomfort. Deep-seated parts should have larger currents administered through large electrodes. When applications are made to any part of the head or neck, additional care must be exercised, the effect upon the brain being very peculiar and unpleasant, especially at make and break. Toleration of large currents is rendered possible by the use of large electrodes to reduce the density of the current per unit of area. With the coil the operator must gauge the strength of the current upon himself first, and should repeat the test with every increase in its strength; a strict adherence to this rule is the best plan, by far, of ensuring the proper amount of caution. Patients, as a rule, are extremely intolerant of painful shocks, and it must be remembered that the very name of electricity is enough to make many patients a little anxious or alarmed on their first trial of electrical treatment.

Duration of Applications.—The usual duration of each application is ten or fifteen minutes.

The number of applications varies very much, usually a considerable number are required. In most cases submitted to electrical treatment one cannot expect a rapid cure, but rather a gradual slow improvement. In some cases of infantile paralysis it may be necessary to continue treatment for several years. As a general rule, it may be said that a month of treatment, with two or three applications a week, will be enough to produce decided improvement, but it is not possible to lay down any precise rules. It is usual for improvement to begin early if the treatment is likely to do good. In that case the patient will be encouraged to persevere. If at the end of a month of regular treatment there is no visible change, or if the improvement has ceased to be progressive, then the treatment may be discontinued.

General Applications of Electricity.—The morbid conditions in which treatment by general electrisation has proved to be of real value have already been indicated in general terms. They comprise (1) simple forms of defective nutrition, such as occur during tardy convalescence after acute illness, and particularly after influenza, diphtheria, and typhoid fever, and after child-birth; (2) rickets; (3) chlorosis and other forms of simple anæmia; (4) neurasthenic states; (5) the disturbances of the nervous system at the menopause; (6) toxic general neuritis from alcohol, arsenic, and lead; (7) certain forms of mental failure, especially those in which the general nutrition is not maintained.

Of a series of cases subjected to general electrical treatment at Claybury, Dr. Robert Jones writes as follows:—"I have tried the electric baths in the case of adolescents mostly. In these and others the form of insanity was that of melancholia, some of the cases presenting well-marked melancholia attonita or anergic stupor." He then proceeds to give details of twenty-three cases which all gained weight, the average gain being 1 lb. a week, and the greatest gains 25 lbs. in one case and 19 in another. After detailing the symptoms of improvement in mental and bodily health shown by his cases, he adds, "I should especially recommend electric baths in melancholia in adolescents, and apathetic cases. Certain puerperal cases of melancholia have also done well."

In chronic gout, chronic rheumatism, and in rheumatoid arthritis treatment by general electrisation is often beneficial, and in some glycosuric states a marked influence upon the quantity of sugar excreted may often be observed.

The General Neuroses.—In this class of affection electricity has been largely used. In the treatment of *hysteria* especially, the application of electricity in almost any form is frequently followed by the happiest results in the way of the disappearance of the symptoms, and if the results are obtained by a psychological rather than by a physiological influence, it is well to bear in mind that electricity is none the less valuable in medical treatment because its effects may be due to an action upon the mind of the patient, for in hysteria some such profound mental impression, acting through the sensory nerves or in other ways, is chiefly required; but the cures effected by its means can only be attributed in an indirect way to the electrical properties of the apparatus employed. Occasionally the mere sight of the electrical apparatus is sufficient to dispel hysterical symptoms.

Electrical treatment, though it may cure the particular symptoms which are present at the time, does not alter the peculiar hysterical tendencies of the patient. In anæsthesia, contractures, paralyses, painful joints, weak spines, aphonia, etc., local stimulation with the induction coil, either with the ordinary electrodes or with the wire brush, should be used. The symptom often departs suddenly during the course of the first sitting, or it may gradually disappear afterwards. It is seldom that more than a few repetitions of treatment are needed, and meanwhile other treatment to improve the patient's general state of health should be adopted. The electro-static machine is also a very useful engine for the treatment of hysterical manifestations.

Chorea.—The cases published in the *Guy's Hospital Reports*, by Golding Bird in 1849, and by Gull a few years later, of the successful treatment of chorea by statical applications are among the classics of electrotherapy. At the present day this disorder very seldom comes within the reach of electrical treatment. The few cases which I have had an opportunity of seeing and treating in this way have been satisfactory, and in some instances strikingly so. In the treatment of chorea by static charging the child should always be held in the nurse's arms upon

the insulating platform. Charging positively is generally sufficient. A brush discharge to the spine may be added if the case improves too slowly.

Insomnia.—Many forms of sleeplessness may be treated by electricity with advantage. An application of induction-coil currents to the trunk and limbs at bed-time will often suffice to induce sleep, as will massage given in the same circumstances. Static or high-frequency treatment may also be used, and the state of the blood pressure should be used as a guide as to the choice of one or other of these methods. With a low blood pressure, the former method should be chosen; with a high blood pressure, the latter will be more successful.

Graves' Disease.—The electrical treatment of this disease has received a good deal of attention, and from time to time favourable results have been obtained and published. Among the more recent publications on the subject is an account by Dr. Rockwell of forty-five cases; the method which he recommends is to use strong electrical currents—twenty, forty, or even sixty milliampères. These are applied by means of electrodes of very large surface; the kathode over the pit of the stomach, and the anode to the nape of the neck. General electrical treatment by the electrical bath, or otherwise, may be used concurrently. Vigouroux has recommended the use of the induction coil, applying it in turn to the eyeballs, the chest, the thyroid, the sides of the neck, and the cardiac region. Other writers advise other operative procedures; there is no certainty of relieving the patient by any of them. Electrolysis of the enlarged gland is perhaps the most promising method.

Local Applications of Electricity.—These have been recommended in a great number of morbid conditions. To justify the use of electricity in the treatment of disease it is necessary that the method should offer results which are superior to those which can be attained in other simpler ways. Unless this condition be fulfilled, treatment by electricity is hardly worth consideration.

In Diseases of the Nervous System.—The striking effects of electrical currents in causing contractions in paralysed muscles has naturally excited much attention. In the whole class of affections of the peripheral nerves, both motor and sensory, electrical applications are of the greatest value for purposes of treatment. Care must be taken to apply the electricity in a suitable manner, for applications suited to paralytic affections may be quite unsuitable in cases in which the relief of pain is the object desired. The principles upon which the selection of a method is to be based have been considered already.

In affections of the spinal cord electricity is useful in some cases, though no method has as yet been devised of arresting the progress of the degenerative diseases which form so large a proportion of spinal cord cases.

In the sequelæ of acute myelitis electrical applications are of undoubted service, and in promoting the recovery and growth of muscles damaged by infantile paralysis they should always be employed, the

treatment being continued for years if improvement should continue to follow its application.

In hemiplegia electricity may be used with advantage during convalescence as a means of hastening the recovery of power in the paralysed limbs. Some improvement may always be expected, although the degree of recovery which can be gained is strictly limited in this disease, as it is in infantile paralysis, by the extent of the original damage done to the nerve centres involved.

The Special Senses.—Electricity has been used in cases of *anosmia*, and successes have been recorded. In *ozœna* the electrolytic introduction of copper ions is said to be a valuable method.

In optic neuritis Erb has reported successful cases, and advises the use of the battery current, with the anode stabile, over the closed eyelids, the kathode being at the nape of the neck. In primary optic atrophy the results are generally negative.

Corneal opacities and anterior *synechia* are favourably influenced by gentle applications to the cocainised cornea; the effect is one of electrolysis, not by destruction of the surface, but by the introduction of chlorine ions, which have a marked effect upon scar tissue. The electrode used is a smooth silver probe, and the polarity must be negative. Electrolysis is also used for its destructive effects in *Xanthelasma palpebrarum*, in the removal of eyelashes in cases of entropion, for stricture of the lachrymal canal and in trachoma, using copper needles.

The muscles of the eyeball cannot be tested electrically with any form of electrode hitherto devised, and it is doubtful whether electrical currents applied to the eyelids have any useful effect upon them for therapeutic purposes.

The Auditory Nerve.—In a certain number of cases the application of electricity produces very good results in cases of nerve deafness, but in the majority it is unfortunately of little or no benefit. In deafness from middle ear disease the results are also not very satisfactory. In tinnitus aurium the results are good or fairly good in a considerable number of cases, but it is difficult to lay down any rules to enable one to pronounce beforehand as to how the treatment may result. It was formerly believed that the nature of the response of the auditory nerve to electrical stimulation might be used as a guide in prognosis, but this is not so. A marked response to a stimulus by the ready production of the sensation of a sound, or by the increase of a sensation of sound already existing, implies an increase of irritability in the auditory nerve, but is not necessarily a good sign. If electricity could be so applied as to modify and correct the morbid changes at work in chronic middle ear diseases, the prospects would be different, but with our present knowledge the attainment of this object seems remote.

The Joints and Bones.—Fibrous ankylosis of a joint, if due to an injury or disease which is no longer active, can be favourably influenced by electrical applications. Leduc, who has drawn special attention to this matter, regards the effect as due to the introduction of chlorine

ions. The negative pole should therefore be applied to the joint, and the electrode should be large and moistened with salt solution. In many instances the monopolar arm-bath method is the most convenient method of applying currents to the joints. The pain and swelling of a recent sprain can be much relieved by applications of the continuous current. Remak has reported some instructive cases of this kind. In hydrops articuli affecting the knee the use of continuous current is useful. Chanoz and Lévêque have reported three cases in which tuberculous joints were much benefited by the treatment. Gonorrhœal stiffness of a joint has also been greatly improved by the continuous current; according to Denoyés, high-frequency applications may also do much good in this condition. In rheumatoid arthritis general electrisation by the sinusoidal bath has a good effect, but not in all cases. It is the best routine treatment, and is superior in its results to ordinary hot-water baths, douches, or massage.

The Circulatory System.—One of the most important observations which have been made upon the effects of high-frequency currents is that they appear to exercise a very marked effect upon the blood pressure in cases of arteriosclerosis. Moutier, after giving much attention to this matter, now states quite confidently that the subjects of arteriosclerosis can be greatly ameliorated if treated by high frequency, particularly if at the same time their dietary scale is properly adjusted. The method he prefers is the cage method of D'Arsonval, or auto-conduction. The static machine has been used to produce the opposite effect, viz. to raise the blood pressure. This it undoubtedly does, and it is the increase in the blood pressure which is the probable explanation of the feeling of well-being experienced by certain persons when statically charged, and of the feeling of discomfort felt by others in the same circumstances. The effect, though probably a transient one, is so marked that it is possible, by observing the behaviour of a patient during the first application, to foresee the probable effect of a course of statical treatment in any given case.

General electrisation has been recommended in the treatment of some forms of cardiac neuralgia, in dilatation of the heart, and in cardiac dropsy. It is considered unsuitable for cases with marked arteriosclerotic changes. Larat has advised the use of the sinusoidal-current bath, and he mentions that improved compensatory changes, decrease of cardiac pain, reduction of anasarca, and freer diuresis have been noticed in cardiac cases treated in this way. Caution should be observed at the commencement of a course of baths, as heart patients may show some dyspnœa or embarrassment of the heart as the result of immersion in warm water. The temperature of the water should not be more than 93° F. at first, and the patient should enter and leave the bath gradually and cautiously.

Electrolysis has been used for the cure of aneurysm of the aorta; the procedure is carried out by the introduction of needles into the sac and the passage of a current. Although successful cases have been reported,

the operation is not free from danger, and may accelerate the death of the patient.

In the treatment of Raynaud's disease and in chilblains electrical applications are useful. Sir T. Barlow has recommended the continuous current for the former disease. The arm-bath and foot-bath methods of treatment are of great value in arresting the progress of chilblains and in warding them off. In all except the most severe cases the induction-coil current or the sinusoidal current should be employed.

The Respiratory Organs.—Very little has been gained hitherto in the treatment of diseases of the lungs by electrical methods. It has been claimed that high-frequency applications have afforded good results in pulmonary tuberculosis, but the same may be said of almost all rational modes of treating this disease ; and the results of high-frequency treatment are not so uniformly favourable as to justify its adoption as a general method. Further study of the subject is necessary. The use of electricity for the generation of ozone to be inhaled in pulmonary tuberculosis may be referred to, as Labbé and Oudin state that they have had good results. Bordier recommends inhalations of ozone for whooping-cough. The static brush discharge is said to have a strengthening effect upon the voice of singers, and to be useful in cases of spasmodic asthma.

The Organs of Digestion.—A condition of habitual dryness of the mouth, with absense of the normal salivary secretion, is occasionally met with, and may be so marked as to render the chewing of a biscuit an almost impossible task. A successful result followed electrical treatment in a case under my care. The continuous current was used. The positive pole, in the form of a moistened pad, was applied over the parotid and submaxillary regions of both sides in turn. A bare metal sound was used as the negative electrode, and was applied to the inside of the mouth, especially to the parts around the orifices of the salivary ducts. Slight improvement soon commenced and gradually progressed until the patient had completely recovered. Œsophageal spasm is a condition which produces troublesome dysphagia, although the passage of a bougie proves that no stricture is present. A short course of treatment by positive static charging, with the brush discharge to the neck, chest, and epigastrium, may dispel the tendency to spasm and enable the patient to swallow with comfort, the improvement lasting for several months when once established.

In nervous vomiting and in reflex vomiting of pregnancy the continuous current acts favourably. The positive electrode is to be applied above the clavicle between the insertions of the sterno-mastoid on the right or on both sides, the negative to the epigastrium. The applications may be repeated hourly.

Treatment by high-frequency applications have been recommended in cases of gastralgia and of gastric myasthenia by Dr. Herschell, and in dilatation of the stomach by Drs. Crombie and Bokenham.

Constipation.—Peristalsis can be set up by electrical currents applied through the abdominal walls, and chronic constipation can be per-

manently relieved by its use. The poles may be placed, one on the lumbar spine and the other on the surface of the abdomen. They should be of large size; the abdominal electrode should be moved over the whole surface of the belly for a period of five or ten minutes. After a few applications the bowels become more regular.

Dr. Herschell recommends the use of three-phase currents for the treatment of constipation due to muscular weakness of the intestinal walls. Two of the electrodes should be applied to the back, one on either side of the lumbar spine, and the third should be at the epigastrium.

Mucous Colitis.—Doumer has stated that the use of large currents of large magnitude applied to the iliac regions through large electrodes has a valuable effect in this disease. Another useful adjunct to its treatment is the use of general electrisation, by means of the electric bath.

In *anal fissure and in piles* the effluve of high frequency has been strongly advocated by numerous writers, and it appears to be of real utility. It does not take the place of surgical procedures in cases where the hæmorrhoidal masses are of considerable size, but in minor cases the relief afforded to the patient by a few applications is undoubted. Doumer has reported twenty-six cases of piles treated by high frequency, all of which were relieved or cured; and others have also written on the treatment of anal fissure by this method.

The Urinary and Reproductive Organs.—Incontinence of urine is a condition in which electrical applications are very often useful. When the trouble is part of a general paraplegia the local treatment by electricity will not be of use unless the condition of affairs in the spinal cord can be improved also.

Incontinence by day, due to weakness of the sphincter, is not at all uncommon in women, especially in such as have borne children, and have a certain lack of tone or relaxation of the perineal region. In these patients a little urine is apt to be expelled involuntarily during any muscular effort, such as coughing, and there may be troublesome incontinence. A few electrical applications will often afford great relief to these patients. The applications should be made by means of a bare metal sound introduced into the urethra, with the indifferent electrode in the lumbar region. The sound should not penetrate into the bladder, because, if it does, a large part of the current will be diverted from the walls of the urethra, where it is required.

Nocturnal Incontinence.—This affection has a totally different pathology to that of the kind of incontinence already discussed. In nocturnal incontinence the patients are able to retain their urine in a perfectly natural manner so long as they are awake, but when asleep the bladder has a tendency to empty itself without awaking them. The condition is due to a persistence of the infantile mechanism of micturition, and the bladder acts during sleep in an automatic way, the controlling centre in the brain not being active enough to maintain its influence during the condition of sleep. As a rule, sleep is very sound in patients who are the subjects of enuresis nocturna.

Electrical applications to the urethra in the manner already described, or to the perineal area, by means of electrodes are often of great utility in the more obstinate cases of this complaint. The patients should also be taught to practise the retaining of the urine as long as possible by day, so as to accustom the bladder to become more tolerant of its contents and to augment the influence of the inhibitory centres by the exercise of their functions.

There is a class of patient with so-called nocturnal incontinence in whom careful questioning will reveal the fact that there is not only a tendency to wet the bed at night, but also a weakness by day. These cases occur almost exclusively in females. When up and about they are unable to retain their urine with comfort for more than half an hour or an hour. If after the lapse of that time they have no opportunity of emptying the bladder voluntarily, pain and spasm come on and the urine is expelled. At night, too, they are obliged either to get up frequently, or else to wet the bed. No local electrical treatment seems to have the slightest good effect upon these cases; and it is therefore very important before giving a prognosis to distinguish them from cases of true nocturnal incontinence, in which electrical treatment answers well.

Electricity has also been used for other affections of the generative organs. In *orchitis* and *epididymitis* the continuous current has been used for its effect in promoting the absorption of exudation by means of electrolysis and the introduction of ions. In some forms of *amenorrhœa* general electrisation is useful; in dysmenorrhœa the static charge with applications of the brush discharge to the loins can be of service. In *ovarian pain* the results of electrical treatment are not often satisfactory. Details of the treatment of these special conditions should be looked for in the special text-books of electrotherapeutics.

The Skin.—Many observations point to the fact that the nutrition of the skin can be markedly influenced by electrical applications. The brush discharge of the static machine, or of the high-frequency apparatus, is now used with success in many chronic affections of the skin, and the literature of this branch of electrotherapeutics is rapidly growing in volume. The Röntgen Rays also have an extensive field of utility in the treatment of the chronic dermatoses, and their applications will be considered in the article dealing with the Röntgen Rays.

Denoyés enumerates the following skin affections as suitable for treatment by high-frequency discharges:—Pruritus, psoriasis, eczema, alopecia areata, lupus vulgaris and lupus erythematosus, acne, and impetigo. In all the technique is similar and consists in the use of the effluve of the resonator given without sparking, from a metallic brush electrode, or of the finer effluve of the "glass condenser" electrodes, which may either be exhausted to a conducting vacuum or filled with water or salt solutions.

When the condition is chronic, indolent, and dry, it may be useful to apply a few fine sparks to the surface by means of a wire brush as well.

Two or three applications weekly and a duration of time not exceeding ten minutes are sufficient.

The effect of the brush discharges of the static machine is similar, though in general the power of static machines is inferior to that of the forms of high-frequency apparatus in common use, and the results obtained are therefore better with the latter method. Doumer and Marquant have recorded cases of eczema and eczematous ulceration treated successfully by the brush discharges of the static machine. The patients were placed on an insulating seat connected to the negative pole of the machine, and the positive pole was connected to a pointed electrode and held close to the affected part. Marquant, in his concluding remarks, says that the beneficial effect was superior to that obtained by any other kind of treatment. It was more quickly produced in those patients whose general health was good than in those who were constitutionally unsound. The local pain, and the congestion and discoloration round the ulcers, quickly disappeared, and healthy cicatrisation commenced rapidly.

H. LEWIS JONES.

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THE X-RAYS IN MEDICINE

By Francis H. Williams, M.D.

The X-rays are of assistance (1) in surgical diagnosis, (2) in medical diagnosis, and (3) in the treatment of certain diseases. It is not possible within the limits of this article to do more than present a sketch of this subject, but in a system of medicine it is, of course, proper to consider the medical more fully than the surgical side. Radiographs are not given because they require special paper, but to illustrate certain points I have used diagrams and tracings made by means of the fluorescent screen; neither are any photographs presented of cases of cancer cured by the X-rays, because they are now well known.

Apparatus

The principal pieces of apparatus needed for X-ray work are a vacuum tube, enclosed in a Rollins box; a static machine or induction coil for exciting the tube; a fluoroscope and photographic plates for purposes of examination; an instrument for measuring the output and for determining the quality of the rays given off by the tube; a stretcher and a suitable chair for the patient.

Static Machine or Induction Coil.—The static machine has the advantage of being independent of an electric main, and of causing a steady light in the tube. On the other hand, it is difficult and annoying to make it work satisfactorily in moist climates. A machine with four revolving plates 76 centimetres (30 inches) in diameter will meet most of the needs of the practitioner; one of this size can be used to make fluoroscopic examinations of the chest and extremities, and to take radiographs of the extremities. For photographing the chest a larger machine is advisable.

Induction Coil.—A coil does not, as a rule, give as steady a light as a static machine; but, on the other hand, it is not affected by moisture. A 30-centimetre coil is better adapted for taking radiographs than a static machine of the size described, but would not be so satisfactory for making fluoroscopic examinations, as the light it excites is not so steady. If the practitioner wishes to take radiographs quickly a 56-centimetre (22-inch) coil is preferable to the 30-centimetre (12-inch) coil. Even the most difficult portions of the body can be radiographed now in one or two seconds if the generator is powerful enough; but a high price must be paid for such apparatus, the tubes must be carefully adjusted, and must be capable of withstanding a strong current. Speed in radiographic work, like speed in a steamship or a railway train, is only attained, beyond a certain limit, by an outlay out of proportion to the cost of accomplishing

the same end in a somewhat longer time. As a rule it is not necessary to take a radiograph in one or two seconds, for if the patient is in a comfortable position he can keep still without difficulty for a minute or longer.

The coil is generally used on a 110-volt direct current, but it can be so arranged as to be run where there is any electric current.

Interrupter.—Some kind of interrupter is necessary with a coil, but there are so many to choose from that it would be impossible to describe them all within the limits of this article. The one devised by Dr. Mackenzie Davidson, of London, is excellent; the one most used in Germany is the electrolytic interrupter of the Wehnelt form.

Adjustable Multiple Spark-Gap.—The spark-gap in series with the tube enables the practitioner to vary the amount of light coming from the tube, and to use tubes of lower resistance than would otherwise be possible. But if a spark-gap several centimetres in length is employed the light may not be as steady as it should be. This difficulty may be overcome, however, by using adjustable multiple spark-gaps, and it is desirable that both a coil and a static machine should be provided with them. The adjustable multiple spark-gap, as its name shows, is made up of a series of small spark-gaps, a larger or smaller number of which can be brought into the circuit, and therefore the light adjusted to suit the needs of the moment, and yet be steady.

Vacuum Tubes.—Vacuum tubes may be of the double-focus variety, which are used on an alternating current, and contain three pieces of metal, the two terminals, namely, the cathode and the anode, and the anticathode or target; or of the single-focus type, which are used on a direct current, and contain two pieces of metal only, one of the terminals, the anode, acting also as the anticathode. Tubes vary in the amount of resistance they offer to the passage of the electric current. This resistance may be measured by ascertaining through how long a distance in the air the current will jump rather than pass through the tube, and the amount of obstacle thus offered to the passage of the current is indicated by saying that the tube has a resistance of so many centimetres or millimetres. Tubes of low resistance give out more rays that are absorbed near the surface, and those of high resistance more rays that penetrate deeply. Rollins has done much to promote the use of the X-rays in medicine by the vacuum tubes and other apparatus he has devised, and by his scientific researches. The results of much of his work and experience are given in his lately published book, *Notes on X-light.*

The practitioner should have a score or two of good tubes, in order that, in a given case, he may be able to choose one exactly suited to his purpose. It is not difficult to find a tube suited to a generator of moderate power, but if a powerful apparatus is used strongly built tubes are required, and the resistance must be precisely adapted to the work that is to be done. Powerful apparatus, therefore, demands time to prepare it for use, and much more experience. If the work of the practitioner requires both high and low tubes, it is more economical to

purchase only the low tubes, and to use these until they become high, than to buy the high tubes.

Rollins Box for Tube.—The tube should be enclosed in a Rollins box, that is, in a box coated with white lead to a thickness of about ½ centimetre (¼ inch), in order that the rays may not escape except where an opening has been made for the purpose. Such a box should have circular openings on three sides, 7½ centimetres (3 inches) in diameter, all of which are covered by lead plates about ½ centimetre (¼ inch) thick, except the one in use, and this one should be covered by an iris diaphragm, as this diaphragm enables the practitioner to enlarge or decrease the opening very easily according to the size of the area to be examined or treated. The box containing the tube may be conveniently supported by means of a counter-weight over a pulley, and so arranged that it may be raised to a height of about 7 feet, easily lowered nearly to the floor, or moved in a horizontal plane from side to side, or in and out. The protection given by this box is essential to the safety of any worker about an X-ray apparatus, or to the patient, and a vacuum tube should never be used without it or some similar protection; but the *dangers of the X-rays* do not seem to be sufficiently appreciated, and this practicable and simple method devised by Rollins, of protecting the observer and the patient, is not in general use. It is true that many persons have used the X-rays for some years without enclosing the tube, and have received no injury; on the other hand, many of those engaged in the manufacture of vacuum tubes or in X-ray work have suffered from slight or serious injuries, some injuries being followed by cancer, which has necessitated amputation of the fingers, hand, or even arm. The eyes also have been affected. Patients likewise have been burned. The latest injury caused by the X-rays, of which I am aware, is the production of sterility, at least temporarily, in men. Eight cases have come to my knowledge in which the failure to have children seemed to be explained in this way. The correctness of this diagnosis is confirmed by the experiments of Albers-Schönberg with guinea-pigs and rabbits, and by the two cases of men described by Philipp. In one of these cases sterility was produced intentionally; in the other the X-rays were used as a therapeutic agent for a skin disease, the patient being warned of the result that might follow. (Philipp recommends the use of the X-rays as a convenient and painless method of producing sterility in men.)

Fluoroscope and Photographic Plate.—Either tungstate of calcium or platino-cyanide of barium screens may be used in the fluoroscope; the tungstate of calcium screens are sometimes phosphorescent as well as fluorescent, only the latter are desirable; the platino-cyanide of barium screens must be renewed from time to time. For examination of the thorax the screen should be 25 × 30 centimetres (10 × 12 inches), for ordinary purposes 20 × 25 centimetres (8 × 10 inches), for some special purposes a very small screen is necessary.

To protect the practitioner from the effects of the X-rays, Rollins has devised a fluoroscope which is made of copper instead of wood, the

fluorescent screen being covered with glass as a safeguard to the eyes. Following along the same lines I have had a fluoroscope made that is protected with copper $1\frac{1}{2}$ millimetre ($\frac{1}{16}$ inch) thick in certain parts, especially at the top of the box and on the handle side, a long sheet of copper extending beyond the handle to shield the hand (see Fig. 15). A piece of plate glass (not shown in the cut) 5 × 10 centimetres (2 × 4 inches) and $2\frac{1}{2}$ centimetres (1 inch) thick, which is bevelled at the edges to fit the interior of the box, is fastened inside the top just below the leather guard for the eyes. The hand, face, and eyes of the practitioner are

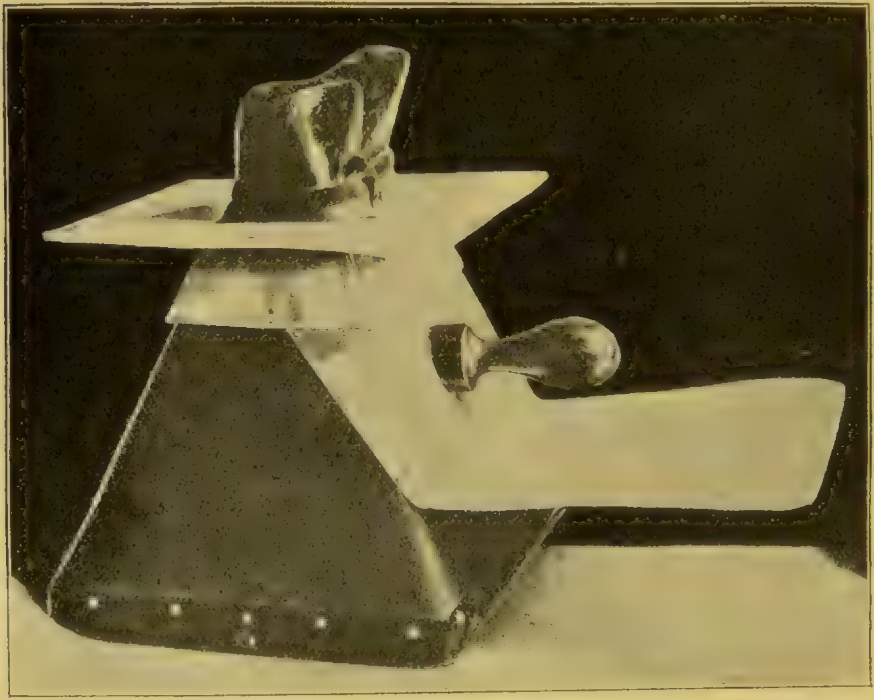

FIG. 15.—Protecting fluoroscope.

thus protected. A long wrister of sheet metal extending to the elbow may also be worn if desired to protect the arm further. With the tube enclosed in a Rollins box, and this protecting fluoroscope, the observer is well shielded from the rays while making examinations with the fluorescent screen. Photographic plates of any good make may be used. It is important that they should be fresh.

Fluorometer.—The fluorometer is an instrument (1) for measuring the amount of rays given off by different vacuum tubes, or the same tube at different times; (2) for determining, in connexion with different thicknesses of aluminium plates, the proportion of rays of high and of low penetrating power that are given off by different tubes, or by the same tube at different times. It consists of a cone of cardboard, which contains

a tungstate of calcium screen on which some radium, enclosed in a sealed glass tube, is lying, the radium[1] being the constant in the tests.

1. The amount of rays given off by any tube may be measured by ascertaining the distance at which the fluorometer must be held from it in order that the light the latter excites on the screen of the fluorometer may equal that given out by the radium lying on the screen. This distance is the fluorometer reading, and all tubes may be compared by comparing the squares of their respective fluorometer readings. For example, if the fluorometer must be held within 4 feet (122 centimetres) of one tube to obtain as bright a light on its screen as the radium gives out, and can be removed to a distance of 8 feet (244 centimetres) from another tube and the same results be produced, we find by squaring the respective fluorometer readings that the amount of rays given off by these two tubes is as 16 : 64. In other words, the second tube is giving out four times as much light as the first. Some tubes that I have tested gave out ten times, or more, as much light as others.

2. The proportion of rays of high and low penetrating power given off by any tube may be measured by comparing the squares of the respective fluorometer readings before and after the interposition of an aluminium plate $\frac{3}{4}$ of a millimetre to $1\frac{1}{4}$ centimetre ($\frac{1}{32}$ to $\frac{1}{2}$ inch) thick between the tube and the fluorometer. For example, if the square of the fluorometer reading of a given tube is 16 feet before the interposition of the aluminium plate and 4 feet after such interposition, the tube is giving out rays three-fourths of which are of such low penetrating power that they are absorbed by the plate. If the squares of the respective fluorometer readings made before and after the interposition of the aluminium plate are, for instance, 16 and 36 respectively, five-ninths of the rays emitted by the tube are rays that are easily absorbed. A tube of low resistance may emit light 75 per cent of which may be absorbed within about $1\frac{1}{4}$ centimetre ($\frac{1}{2}$ inch) of the surface of the body, whereas only 10 per cent of the rays of a tube of high resistance may be thus absorbed; yet the total amount of rays of low penetrating power given out by the second tube may be greater than that emitted by the first. The importance of testing tubes by means of the fluorometer is evident.

The following curve indicates the proportion of rays of different degrees of penetration emitted by a tube of low resistance, as determined by fluorometer readings taken before and after the interposition of aluminium plates, the total thickness of which varied from $\frac{1}{64}$ of an inch to $\frac{28}{64}$ of an inch. The total amount of light issuing from the tube is

[1] Specimens of radium vary in brightness, and therefore until some substance that has a uniform brightness is adopted for all fluorometers, the brightness of the radium used must be measured by a photometer in order that the readings of different fluorometers may be compared; or better, all fluorometers can be compared with a special fluorometer in order to standardise them. Thus if it is known that one fluorometer is to another as 1 : 2·3, for example, their readings can be compared. Any fluorometer may be employed as the standard for one clinic without reference to other fluorometers. Some less expensive source of fluorescent or phosphorescent light than radium, for a standard of measurement in the fluorometer, is desirable; but, fortunately, only the cheaper strengths of radium are necessary for this purpose, and the amount required is not large.

indicated by the figure 2560, the square of the fluorometer reading taken before the interposition of any aluminium plate. Tubes vary very much, as already stated, in the total amount and in the quality of the light they give out.

Stretcher and Chair.—A stretcher supported about 76 centimetres (30 inches) above the floor on two wooden horses makes an excellent examining table. It has the merit of simplicity, and is adapted to most

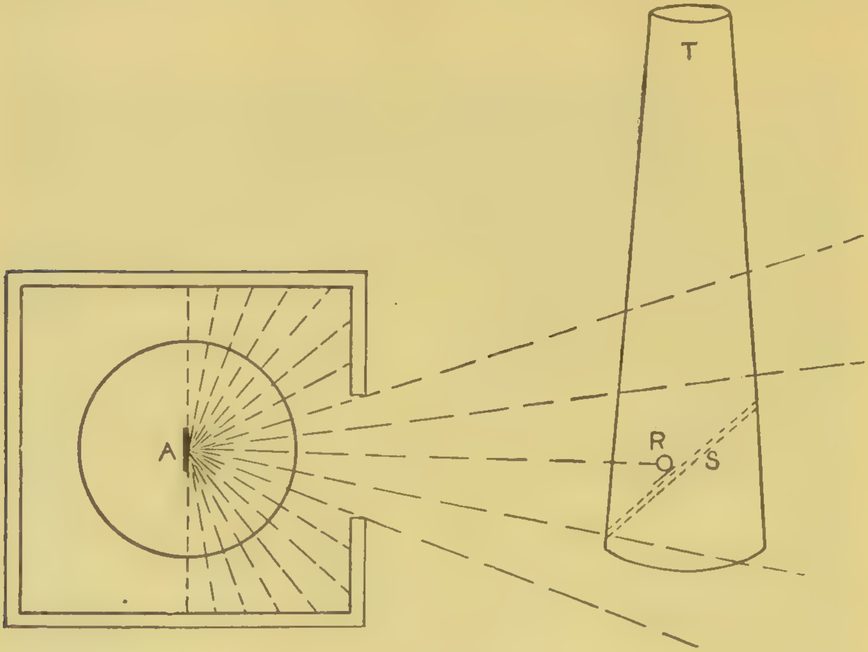

FIG. 16.—Fluorometer. From the third edition of *The Roentgen Rays in Medicine and Surgery*. Instrument for determining the amount of fluorescence produced by different vacuum tubes, or the same tube at different times, on the tungstate of calcium screen. The cut shows the section of a Rollins box and of a vacuum tube, the anode of which is at A. The broken lines originating at A represent the rays given off at the anode. At the right of the cut is shown a cardboard tube T, the interior of which is black, and in the lower end of which is a small oval screen S of tungstate of calcium; across this screen is fastened a sealed glass tube R, 8 centimetres long, containing some radium, and under it a strip of thin cardboard. This screen has been put at an angle in the tube in order that the instrument may be used without exposing the eye and hand to the X-rays. To determine the amount of fluorescence produced on the tungstate of calcium screen by a given tube, the room should be darkened; the tube T should be held near the top, its opening, the rim of which is made soft by a covering of velvet, placed close to the eye, and its other end at such a distance from the anode of the vacuum tube that the radium appears as a bright band on the less bright screen; then the cardboard tube should be brought gradually nearer the anode until a point is reached at which the amount of light from the radium R and the screen S is about equal (or the point when the band of light from the radium is just disappearing may be chosen). The distance between the radium and the anode should then be measured and noted.

purposes. When a stretcher is used the tube is generally placed below the patient, which is an advantage. For instance, if a fracture is in question, the fluoroscopic examination can first be made, then, without moving the patient or the tube, the light can be turned off for a moment and a photographic plate, enclosed in light-proof envelopes, be placed over the part a radiograph of which is desired. By this method the comfort of the patient is assured, and there is no risk of breaking or injuring the

plate by pressure. If the practitioner desires to examine the patient in

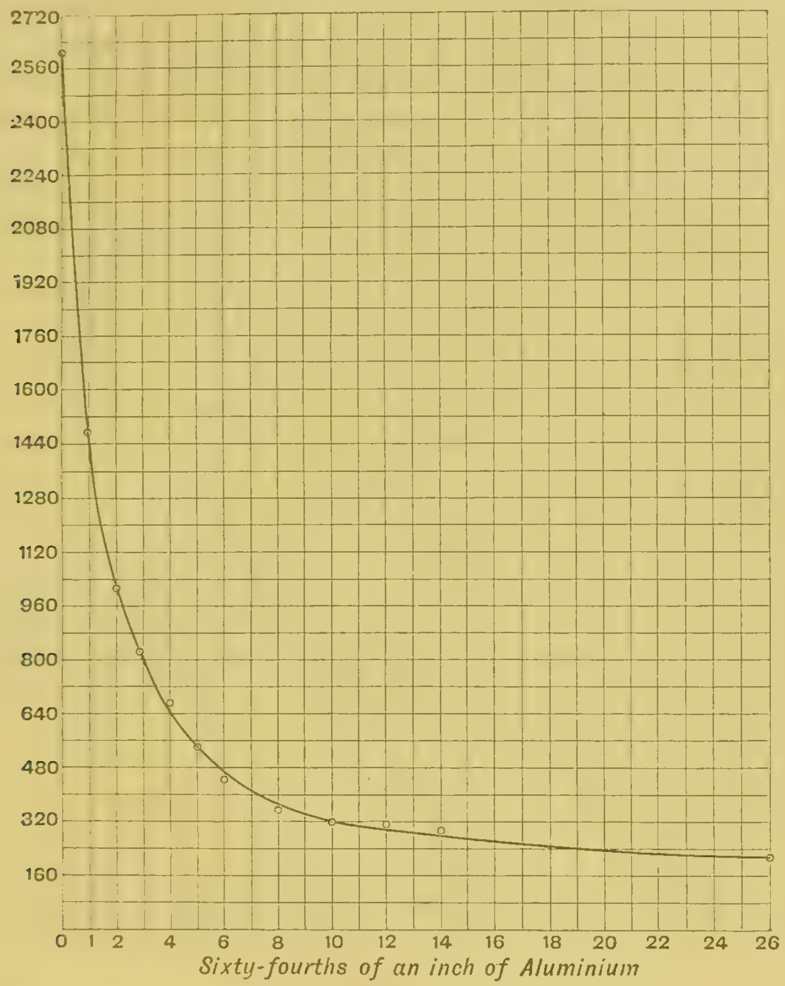

FIG. 17.—Curve showing the amount and quality of X-light emitted by a vacuum tube of low resistance. The figures on the vertical line are the squares of the fluorometer readings of a tube of low resistance; the figures on the horizontal line give the different thicknesses of aluminium which were interposed between the tube and the screen of the fluorometer when all but the first fluorometer reading were taken. The curve shows the large proportion of rays of low penetrating power that was given out by this tube and the composite character of the X-rays.

a sitting position, the latter may be seated on a revolving chair or stool that can be turned while the fluoroscopic examination is being made.

Surgical Uses

One of the earliest uses of the X-rays was the localisation of foreign bodies, such as bullets and coins, whose density is greater than that of the tissues of the body. Foreign bodies light in weight, such as splinters of pine wood, are not so easily detected by the X-rays.

Methods of Examination.—The general directions in regard to the distance of the tube from the plate or screen, the angle at which the rays should strike them, etc., etc., are given on p. 487.

Localising foreign Bodies.—Metallic foreign bodies can frequently be seen by means of the fluoroscope, and their position can be determined as follows: With a crayon suitable for marking on the skin, contained in a brass tube, the practitioner marks a dot on the anterior and posterior surface of the body at the point under and over which the screen shows that the embedded object lies. He then either turns the patient or moves the tube so that the light will go through the body at an angle of about ninety degrees to the first direction, and marks the skin again at the point over which the object lies, both on the side nearer the tube and on that farther from the tube. It is obvious that the foreign body will be found at the point where the line joining the first two dots crosses the line connecting the second two dots. I believe this is the simplest way of localising foreign bodies, and, so far as I am aware, it was used first by me in April 1896 at the Boston City Hospital. There are other methods of accomplishing this result, but they are more cumbersome.

Mr. Mayou has suggested a means of withdrawing foreign bodies of iron or steel from the stomach by the aid of the fluorescent screen; Hamilton has advised that when a foreign body is to be removed from the œsophagus the instrument used be guided by means of the screen, as he has known two cases in which a coin was driven through the wall of the gullet after it had been located by the X-rays and the patient removed to the operating room. The stereoscopic fluoroscope may also be used to locate foreign bodies. Dr. Mackenzie Davidson and E. W. Caldwell have each devised such an apparatus.

If the foreign body cannot be easily seen with the fluoroscope, radiographs must be taken, and these may be made by the excellent method devised by Dr. Mackenzie Davidson, or the stereoscopic method may be used. Several ingenious forms of apparatus have been devised for locating a metallic body in the eyeball. I would call attention to the one devised by Sweet, and to that by Fox.

Fractures.—It is no longer necessary to urge the importance of making radiographs of fractures, for the profession has accepted their use as an essential part of the examination. Radiographs not only enable the surgeon to recognise fractures which would not otherwise be suspected, but sometimes they can assure him also that the suspected fracture does not exist. Recently a woman 70 years of age was brought into hospital after a fall, and the diagnosis of a fracture of the neck of the femur was made. The radiograph, however, disclosed that the femur was uninjured, but that the ilium on that side was broken; the radiograph further showed that the bladder contained five calculi, one 4 centimetres by $2\frac{3}{4}$ centimetres, and four small ones. Moreover, radiographs have enabled the surgeon to treat fractures in a more intelligent way than has hitherto been possible. Ross and Wilbert, Dent, and others have done excellent work in the examination of fractures by the X-rays.

Method of Examination.—It is important that the position of the tube with reference to the part of the body radiographed should be recorded on the photographic plate. It is also sometimes important that two views should be taken of fractures of the extremities without moving the part, but only the tube, one from an antero-posterior and the other from a lateral point of view. It is a simple matter to have a frame made that will hold the plates in each of the desired positions while a radiograph of a leg or ankle, for instance, is taken. An excellent frame for this purpose is used at the Salpêtrière in Paris. By means of these two views the surgeon not only gets a better appreciation of the conditions present than would be possible with one view alone, but is also prevented from failing to recognise a fracture, an event that might occur if one view only were taken. Another means of obtaining a clear conception of the conditions present in fractures is to take stereoscopic views, and then place the negative in a simple form of reflecting stereoscope.

For the study of fractures every hospital should have a series of radiographs of the extremities, and especially of the joints, of normal individuals of different ages. It has sometimes happened that the ununited epiphyses normal in youth have been interpreted as fractures.

Diseases of the Bones.—Radiographs of diseased bones are worthy of careful study, as they are of use in making a diagnosis in osteomyelitis, tuberculous and post-typhoid disease of the bones, osteosarcoma, abscess of the bones, and syphilitic disease of the bones; and certain of these diseases can be recognised in an earlier stage than would be possible without the detailed picture the radiograph gives. Some diseases of the bones, which would otherwise be entirely unsuspected—for example, diseases of the ribs—can be clearly shown by radiographs. The value of radiographs in diseases of the spinal column is noteworthy. Space does not permit me to describe the appearances which are characteristic of these diseases, nor would it be possible to give a clear presentation of this important subject without a series of radiographs more carefully reproduced than is possible in the ordinary half-tone.

Renal Calculi.—Mr. Macintyre, of Glasgow, was the first to show that a renal calculus could be recognised in a radiograph. Since his article was published other practitioners have followed in this field, and have obtained results which previously would have been thought by many unattainable. Dr. Mackenzie Davidson has brought this method of examination to wonderful perfection; Albers-Schönberg in Germany has developed it by special devices of his own, and Leonard in the United States has been a most conspicuous and successful advocate of it. He has shown that a considerable number of calculi are found in the ureters. All observers agree that some calculi are more readily detected than others; those which contain salts of calcium, such as oxalate of calcium, or phosphates, are most easily seen; those made up of pure uric acid, on the other hand, are very difficult, or even impossible, to locate by means of radiographs. Fortunately such calculi are uncommon.

If two good negatives have been obtained, both of which show the soft parts clearly, and present appearances characteristic of calculi, the diagnosis may be regarded as established with considerable certainty; when no evidences of calculi are found on the plate, there is probably no calculus present, unless it be one made up of pure uric acid, which would not cast a marked, if any, shadow on the plate.

Method of Examination.—Only the points of most importance in the method of examination can be given here. The patient should have a good movement of the bowels the day before the radiograph is to be made, and no meal should be taken for some hours previous to the examination. The patient should lie flat on his back, with the photographic plate under and the tube above him, when the kidneys, ureters, and bladder are to be radiographed, and sometimes with the tube under and the plate above him when the bladder is radiographed. In order to determine whether a small calculus is in the lower end of the ureter or in the bladder a second negative may be necessary, with the patient lying on his side and the bladder partly filled. Under these conditions, if the calculus were in the ureter the position of the shadow in the first and second negatives would be the same; if the calculus were in the bladder the position of the two shadows would be different, as the calculus would move when the patient changed his position.

It is important that the plate should be in contact with the skin of the patient, for if any clothing intervenes a button might be mistaken for a calculus. The skin, too, should be carefully examined, for if there were any growth on it error might again result. I recall a patient who had a small fibroma, 2 centimetres in diameter, hanging by a pedicle from the skin about over the left kidney. The radiograph taken showed what seemed to be a renal calculus, and another indicated the same. That the appearance on the plate was not due to a calculus, but to the fibroma, was determined by a careful comparison of the latter's size, shape, and position with that of the appearance on the negative. When the kidneys are being radiographed, Albers-Schönberg places a cylinder with a rounded edge under the patient's ribs to press down the flesh; as this diminishes the thickness of the parts intervening between the tube in front of the patient and the photographic plate under him. I use a rubber bag filled with air (see page 510 for description of method).

The tube used for radiographing calculi should be of such a character that, for example, the soft parts are well differentiated, and that some of the muscles of the back and the kidneys are recognisable on the plate. Under these conditions the part of the kidney in which the calculus lies may sometimes be indicated. I prefer, when taking radiographs of calculi, to use a tube of rather low resistance, although it necessitates a longer exposure, that is, one of five minutes or more.

Gall-stones composed of organic matter only would not be recognised by the X-rays; those containing inorganic constituents, such as lime salts, might cast sufficient shadows to show on a negative, but not on the fluorescent screen.

Head.—The contrasts seen in the head are well marked in some parts, and a good radiograph of the head taken with the plate on one side shows even the outline of the external ear on that side. Abnormal conditions of some of the bones of the skull and face may be readily determined; the bones at the base of the skull, as well as those of the vertebræ, may likewise be shown. Schüller's *Die Schädelbasis im Röntgenbilde* is of interest in this connexion. A few cases in which tumours of the brain have been recognised during life have been reported. (Church; Mills and Pfahler; Mills, Pfahler, and Deaver; Straeter.) Stereoscopic negatives assist the practitioner in making a diagnosis of deep-seated lesions of the head and neck.

The X-rays are also useful for examining the frontal sinus. By means of the fluorescent screen the movement of a metal sound can be watched and its direction guided.

Teeth.—The X-rays are valuable for obtaining information about unerupted teeth, for determining the presence, cause, and extent of alveolar abscess, for detecting fractures of the roots caused by blows or falls, and also for other conditions.

Method of Examination.—A method for photographing the teeth was devised by Rollins in 1896. The sensitive films, enclosed in a thin bag of soft rubber or black waterproof paper to exclude light and moisture, are placed inside the mouth. The films are separated by a thin sheet of foil, and several are used, because by this means each one has a slightly different exposure. The tube is placed opposite the same jaw as the films at the distance of about 28 centimetres (11 inches).

Medical Uses

The medical uses of the X-rays are of growing importance, but as yet comparatively few physicians appreciate their value in this field. They give the practitioner a more exact view of the conditions present in many obscure cases, especially of thoracic diseases, because in these cases, for example, the difference in the movements of the diaphragm in health and disease, and the contrast between the light normal pulmonary area and the dense heart, or between the sound and the diseased pulmonary areas, afford a basis for a method of examination that adds confirmatory evidence, and thus makes a firmer foundation for a diagnosis in some cases; while in others they enable us to carry our examination to a point beyond the reach of any other method, and make a diagnosis practicable in an earlier stage of the disease than would otherwise be possible. Early pulmonary tuberculosis is an example of the value of the X-rays in both these two groups, for when our suspicions of this disease have been aroused a diagnosis can frequently be made with more assurance and earlier by the aid of an X-ray examination than is possible without it, or in cases where there is an inherited tendency to tuberculosis, and therefore a precautionary X-ray examination is made, this may give us the first warning of the disease. Thoracic aneurysms are a good illustration of the

second group, for by means of the X-rays this disease may be definitely recognised at a time when, without their aid, it would remain unknown; in other cases they enable us to relieve the patient of his anxiety, and permit him to disregard the precautions which a definite or even a

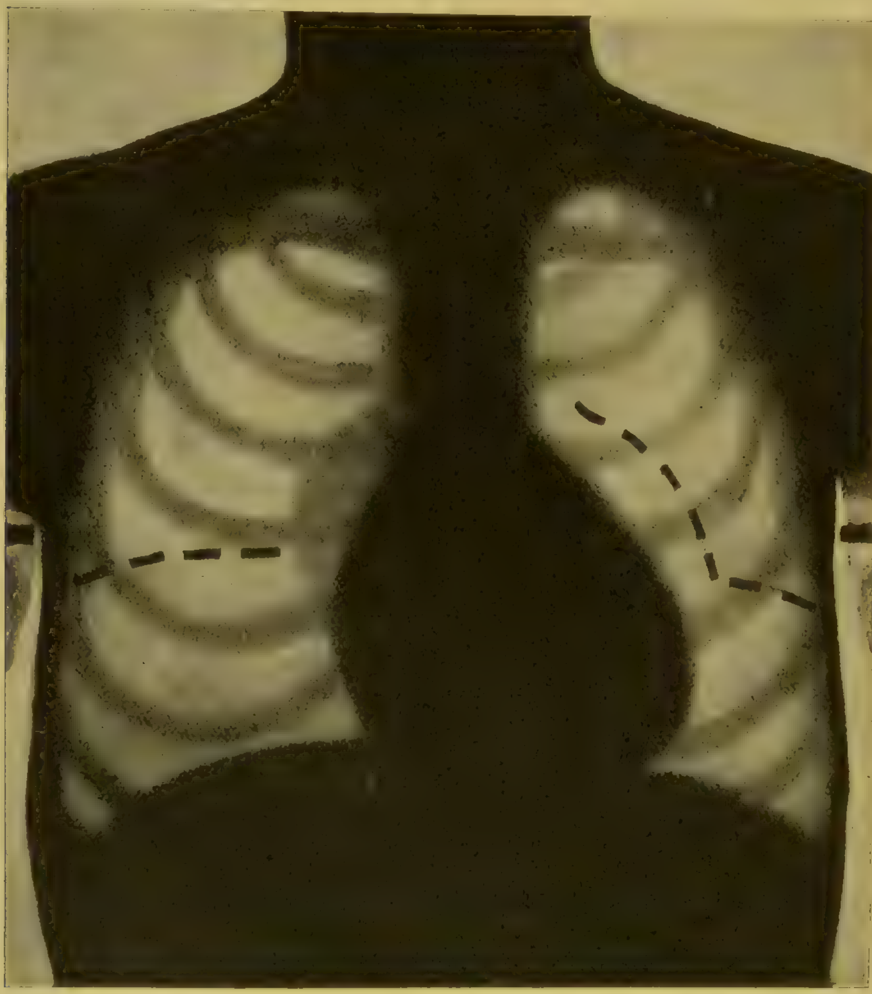

FIG. 18.—The broken lines show the position of the diaphragm and heart in expiration, but the diagram does not indicate that during this time the light pulmonary areas are narrower. The level of the nipples is indicated by the dark lines at the sides of the cut and near the axillæ. The target of the vacuum tube would be placed under the median line, where it is crossed by a line joining the nipples, to obtain such a picture. (From the author's work, *The Roentgen Rays in Medicine and Surgery.*)

probable diagnosis of aneurysm, based on symptoms, would impose. I have been able, quite as often, to assure patients or their physicians that their fears of a thoracic aneurysm were groundless as to tell them that the X-ray examination confirmed the previous diagnosis.

The abdomen offers fewer opportunities for diagnosis by the aid of

the X-rays, and the method is more difficult to carry out, as the contrast in density between the different organs is not so marked as in the thorax.

Thorax.—The most important field for medical diagnosis by means of the X-rays lies in the thorax. The appearances of the normal chest, from an antero-posterior point of view, are shown in Fig. 18. The lungs appear as light spaces, and the heart and diaphragm

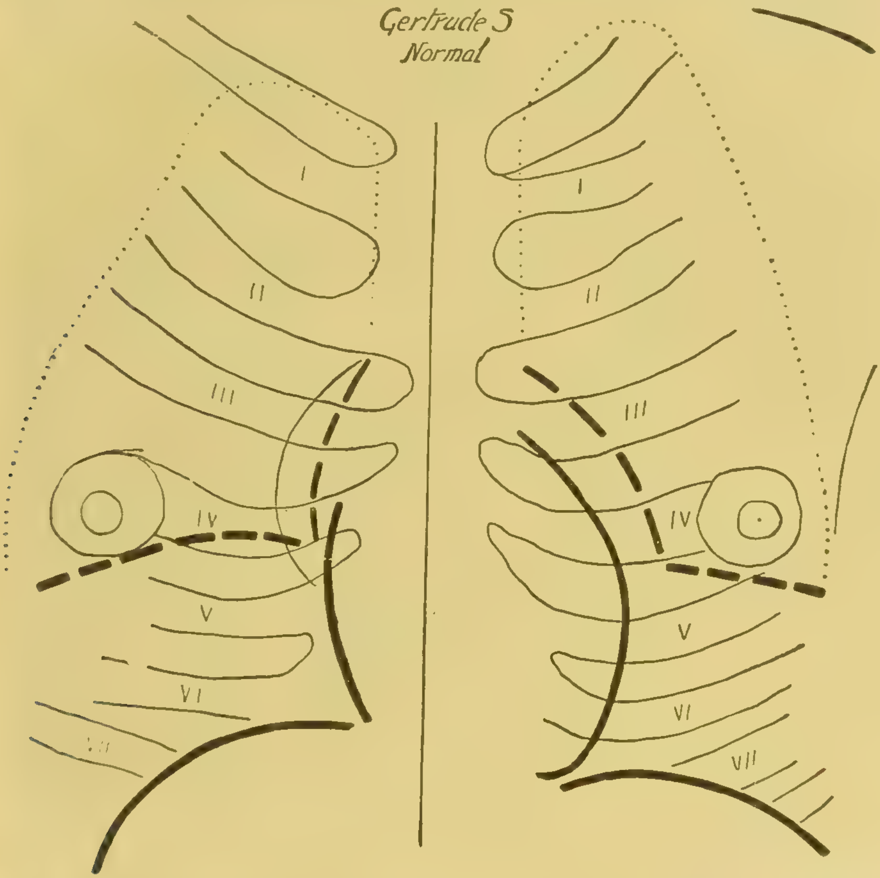

FIG. 19.—These outlines are reduced photographically from the tracing made of the outlines drawn on the front of the patient's thorax. The full lines indicate the position of the heart and diaphragm in deep inspiration; the broken lines in expiration; the dotted line shows about the limit of the bright pulmonary area. The ribs on the back are not shown, as they would confuse the picture. The target of the vacuum tube was placed under the point where the line joining the nipples was crossed by the median line. (From *The Roentgen Rays in Medicine and Surgery.*)

as dark bodies. The excursion of the diaphragm and the movement of the heart from full inspiration to expiration are indicated respectively by the broken lines parallel with the diaphragm and the broken line parallel with the left border of the heart.

The outlines of the heart and diaphragm traced on the skin by means of the fluorescent screen in inspiration and expiration are seen in Fig. 19.

If the patient is turned and the light allowed to go through the chest from side to side, instead of from back to front, the appearances indicated in Fig. 20 will be brought into view. The most striking portion of this tracing, drawn by means of the fluorescent screen, is the light space, usually triangular in shape, which is behind and below the heart. The sides of this triangle are formed by a portion of the posterior border of

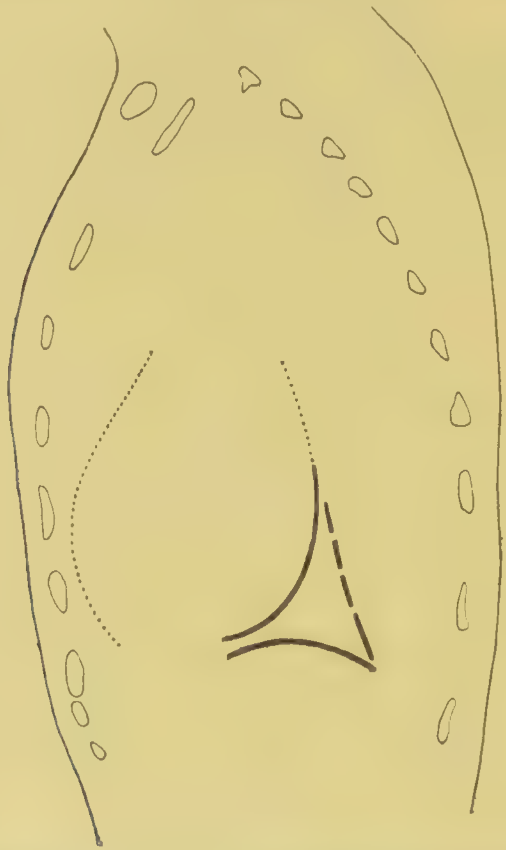

FIG. 20.—The outline of the body and the ends of the ribs have been traced from an anatomical plate, which represents a section of the body through the left parasternal line. The heart line and the outlines of a portion of the diaphragm and spine, or rather what lies in front of the spine, form the triangle, and were drawn on the skin, together with the remaining heart lines, while looking through the patient during full inspiration with the fluorescent screen placed on the left side. These lines were then transferred to the drawing from which this cut was made. The outline of the heart is indicated in the cut partly by a full and partly by a dotted line. The full line shows the extent of the lower and posterior border usually seen in health on the fluorescent screen; the dotted line, the additional amount seen in this individual in health. (From *The Roentgen Rays in Medicine and Surgery.*)

the heart, of the diaphragm, and of the tissues in front of the spine respectively. A wedge-shaped light area, not shown in the cut, the base of the wedge being uppermost, may be seen on the fluorescent screen above the front of the heart and behind the sternum. The heart is sometimes so near the front of the chest, that with the light still in the same position, the whole of its posterior border may be followed during

full inspiration, or so far from the front of the chest that the whole of its anterior border may be easily seen.

Methods of Examination.—Many methods have been devised for examining the chest, some of which require complicated apparatus, while others demand only simple forms. I believe the latter are best adapted for general use, and are most suitable for discussion here. Both the radiograph and the fluorescent screen are of service in examining the chest; although in most cases the screen is preferable, in some both are necessary. The photographic plate gives some details which the screen does not afford; but the screen has the advantage of showing the parts in motion, and the practitioner, by noting the differences in the picture presented during the respiratory cycle, including deep inspiration, can see and learn much that would not show on a photographic plate. Moreover, by turning the patient, and allowing the light to go through the body from different directions, he can observe the parts from different points of view. Further, the practitioner is not obliged to wait, as is necessary when a radiograph is taken, for the development of the photographic plate, but obtains his results directly; on the other hand, he must be skilful in the use of the screen, whereas the radiograph can be taken by a good photographer, although the physician must be able to interpret it. In both methods certain cardinal points must be borne in mind. *First*, unless the vacuum tube is at the proper distance from the plate or screen, the shadows seen upon them will be misleading, because they will not represent with accuracy the size of the objects which caused them. A distance of 70 centimetres ($27\frac{1}{2}$ inches) is usually sufficient. The light should strike the screen or plate as nearly as possible in a direction perpendicular to its surface. It is well also, for purposes of comparison, to have the vacuum tube at a uniform distance from the plate or screen. *Secondly*, the position of the tube with regard to the patient should be recorded when a radiograph is taken or a fluoroscopic examination made, in order that the results of examinations made at different times of the same or different patients by the same or different physicians may be compared. To this end a small bit of metal, such as a metal washer about $\frac{1}{2}$ centimetre ($\frac{1}{4}$ inch) in diameter, should be put on the photographic plate at a point directly opposite the anode of the tube when a radiograph is taken. In the case of an examination with the fluorescent screen, some definite point should be chosen opposite which the anode of the tube should be placed, as a general rule. I have selected for the chest the point where the line joining the lower borders of the fourth ribs crosses the median line of the sternum, that is, in men, the nipple line. In women, these two lines are often not coincident, and in such cases the former of the two must be used. If a very accurate determination of the diameter of a large object is desired, the tube may be first placed under one border, and this determined, and then placed under the other and that obtained. (See page 504.) It would be advantageous if, by some international agreement, a standard of distance could be fixed upon for the tube, and for its position, with reference to the

patient when a radiograph or a fluoroscopic examination of the chest is made; for if such a standard were adopted by all practitioners, the conditions existing at one examination could be compared with those obtaining at another, and any changes that had taken place in the interval could be intelligently measured and appreciated, even if the successive examinations were made by physicians living in different countries.

FIG. 21.—Shows the method of drawing the outlines on the patient's skin while looking through the fluoroscope. The fluoroscope is held farther away from the patient than is necessary in practice in order that the pencil which is under it may be shown in the picture. The observer usually stands on the patient's right, but in order to show the method of examination better, he is seen standing on the patient's left. The box, lined with white lead, enclosing the tube, is seen below the stretcher. The diaphragm, which is placed under the patient's chest in order to obtain a better definition of the outlines, does not show in this figure. (From *The Roentgen Rays in Medicine and Surgery*.)

Many patients can be most comfortably and satisfactorily examined in the prone position, and many kinds of tables have been devised for this purpose, but I think a canvas stretcher answers well. It should be supported, as already stated, about 76 centimetres (30 inches) from the floor, so that the tube may be placed under it, and yet be at a sufficient distance from the patient.

Fig. 21 indicates the method of making an examination of the chest with the fluorescent screen when the patient is in a prone position.

The patient is lying on one of the regular hospital stretchers, on which he has been brought from the ward to the X-ray room, and from which he is not moved from the time he leaves his bed until he is returned to it. The poles of the stretcher rest in notches cut in the wooden horses which support it at either end. The vacuum tube in the Rollins box is placed below the patient, and its anode is 70 centimetres (27½ inches) distant from the fluorescent screen, and is directly opposite the point where the median line crosses the line joining the lower borders of the fourth ribs (the nipple line). This point is obtained by means of plumb lines. The first pair hang from the middle of the wooden horse at the head and foot of the stretcher respectively, and indicate the median line of the stretcher. When the patient has been arranged, with his median line directly over that of the stretcher, a cord, 150 to 180 centimetres long, with a small weight at either end, is put across his chest on a level with the nipple line. The two ends of this line hang down on either side, as seen in the figure, and form a second pair of plumb lines. The physician then sights from one end to the other of the first pair of plumb lines, and places the anode on the imaginary line connecting them; he then sights from end to end of the second pair of plumb lines, and moves the tube until the anode is at the point where the imaginary line connecting them crosses the other. A metal diaphragm may be held under the chest of the patient and moved, as desired, while the examination progresses, in order to improve the definition of the outlines seen on the screen. The physician is provided with a pencil, that marks the skin easily, for drawing the outlines. It is held in a metal holder, or has a strip of metal along its length, because, as this metal casts a shadow, the practitioner is able by this means to follow the point of the pencil as he draws. Crayons, in brass tubes, such as actors use for emphasising the eyebrows, are also very satisfactory.

The appearances seen in the chest may be drawn on a thin sheet of glass, or a film of celluloid, either without the removal of the clothing, or, better still, on the skin, as shown in Fig. 21. If the first method is employed, a metal rod, covered with rubber, should be placed over the sternum in the median line, and other pieces of metal over the nipples, as points of reference, and their shadows marked on the glass or celluloid, so that tracings made at different periods may be compared. In the second case, that is, when the outlines are drawn directly on the skin, a mark should be made over the sternal notch and another over the ensiform cartilage to indicate the median line. The outlines desired should then be drawn on the chest, and should be gone over a second time to avoid any possibility of error. When this process is completed a piece of tracing cloth or paper, about 30 centimetres (12 inches) square, across the middle of which a line has been ruled, should be placed on the chest; the line on

the cloth or paper falling directly over the median line of the body. The sternal notch, second rib, ensiform cartilage, and the nipples should be indicated on the cloth as points of reference, and the tracings on the skin should be traced on the cloth. The name and age of the patient, the diagnosis, etc., should subsequently be added to the tracing cloth, as it then becomes a more complete permanent record. The making and recording of the examination usually takes about ten minutes.

For examination in a sitting position with the fluorescent screen the swivel chair, already mentioned, which has a high leather back, is convenient, or the back may be only about 30 centimetres (12 inches) high. The seat of the chair should be 50 centimetres (20 inches) or more above the floor. The physician's chair should be a low one, the seat about 36 centimetres (14 inches) high. This height would bring the eyes of the physician about on a level with the patient's heart. The proper position for the tube may be determined, as shown in Fig. 22, by means of a level, or the patient may be placed in the chair directly opposite the tube, the distance of the lower border of his fourth rib above the floor being measured by means of a stick, and then the tube placed on the same level. As the chair can be turned, the patient can be examined with the light going through the body in all directions in a horizontal plane. When the examination is to be made with the light going through from side to side, it is well to direct the patient to cross his hands above his head. If, when the light is going through the chest at an angle, one position is found at which some object can be especially well seen, it is desirable to know what this angle is. This may be ascertained by means of a pointer which is fastened to the seat of the chair and turns with it, and a graduated circle, which rests on the feet of the chair and remains stationary. The circle is set with the zero under the pointer when the patient is sitting with the tube squarely behind him, and when the chair is moved the angle at which the light is going through the body can be determined by reference to the number on the circle over which the pointer lies.

There are some conditions, as, for instance, when an examination is to be made of the arch of the aorta for a possible aneurysm, in which the tube may be placed above the nipple line (see page 487), and others when it should be placed below, as, for example, when the triangle which is behind and below the heart is to be looked for. This triangle, as stated on page 486, is seen in full inspiration with the light going through the body from side to side. In some cases, too, it is important that the tube should be placed for a moment on a level with the patient's head, and again as low down as the hip-joint. The examination made with the tube above and below the middle of the thorax makes it possible for the practitioner to recognise the presence of pus or serous fluid between the lobes of the lungs, which might be readily overlooked were the light always kept in a plane on a level with the middle of the thorax; because if the light went through a thin layer of interlobar fluid only, the shadow produced on the screen might be too faint to be recognised, but with the

tube in such a position that the light penetrated the fluid or dense mass edgewise, the shadow would be darker, and therefore more evident. Examinations can be readily made with the tube placed in these different positions, because, as already said, the vacuum tube, arranged in the

Fig. 22.—Illustrating the method of determining any horizontal angle at which the light passes through the body. TS, thumb screw; R, ring; B, bullet; T, tube-holder with iris diaphragm; P (under the chair) indicates the zero of the graduated circle on the disc which rests on the legs of the chair, and may be turned by hand on them. The pointer is fastened to the seat of the chair, and turns with it. For many reasons a chair back, about 30 centimetres (12 inches)

Rollins box as described, is free to move up and down, in and out, and from side to side. Béclère has emphasised the importance of examining the thorax with the tube placed much above and below the middle of the chest.

The *Moritz orthodiagraph* is an apparatus so arranged that when the

fluoroscope is moved in either a vertical or a horizontal plane, the vacuum tube moves with it; thus they are kept automatically opposite each other when the practitioner moves the fluoroscope while examining the patient. The orthodiagraph is also furnished with a pencil which records the outlines of a given organ by a series of dots. The part of the body opposite which the tube has been placed during a given examination may, of course, also be thus recorded.

FIG. 23.—Stereoscopic fluoroscope. A, revolving disc 91 centimetres (3 feet) in diameter; C, small revolving disc; B, shaft with two universal joints connecting discs, so that the fluoroscope F can be moved into any desired position while the apparatus is in motion. This shaft may also be shortened or lengthened at will while the apparatus is running. The vacuum tube (not seen in cut) is behind disc A, and has two anodes about 8 centimetres (3 inches) apart. In arranging the apparatus for use the disc C should be so turned that when one of the openings near its edge is opposite the right eye, the light from the tube should be passing out through one of the openings near the centre of disc A, and when one of the openings near the centre of disc C is opposite the left eye, the light should be passing out through one of the openings near the edge of disc A. The observer sits in the vacant chair, which is lower than usual, and thus his eyes are brought about on a level with the fluoroscope.

The stereoscopic fluoroscope may become a useful means for examining the chest. Such fluoroscopes, as already mentioned, have been devised by Drs. Mackenzie Davidson and E. W. Caldwell. The one shown in Fig. 23 is a modification I have made. It consists of a large disc A, 91 centimetres (3 feet) in diameter, which is opaque to the X-rays, and a

smaller one C, which revolve together. The shaft B connecting them has two universal joints, in order that the fluoroscope F may be moved about, and is driven by a small motor near the base of the wooden upright, to the side of which the shaft B is attached. Behind the disc A is a vacuum tube, which has two anodes about 8 centimetres (3 inches) apart, and as the disc A revolves, the part of the body in front of the fluoroscope is illuminated first by one and then by the other anode. There are three sets of openings in each disc, so that when the discs are turned at the rate of 400 revolutions per minute, there are 1200 flashes of light on the screen. This number of revolutions per minute is sufficiently rapid to give a steady picture.

To do good work with the fluorescent screen, *first*, the light must not be too strong; *secondly*, it must be perfectly steady; and, *thirdly*, it should be controlled by an adjustable multiple spark-gap so that it can be turned up or down at pleasure while examining the patient. Examinations with the screen in diseases of the chest are more important than those with radiographs.

Reference to many refinements both in methods of examination and in apparatus must be omitted for want of space.

Diseases of the Chest

Pulmonary Tuberculosis.—In this disease (1) the excursion of the diaphragm is shortened, the restriction occurring usually in the lower part of the excursion, on one or both sides, of the chest if both lungs are diseased, or if the disease is so advanced that the lower part of the lung is dense, the diaphragm is obliterated on the abnormal side; (2) the diseased portion of the lung or lungs is darker than normal, owing to the increase of density—in the early stage this area is usually the apex and more often the right one—but the restricted excursion of the diaphragm may be seen in some cases before any shadow of the lung is observed on the screen; (3) if one lung only is diseased the heart may be drawn to the affected side, especially during deep inspiration, but the greater excursion of the diaphragm on the normal side would contribute towards this displacement at this part of the respiratory cycle.

Fig. 24 illustrates the appearances seen on the fluorescent screen when only one lung is diseased.

Instead of the signs just mentioned, the practitioner may observe only that the lungs as a whole are less bright than normal, and that the outlines of the ribs are less distinct. This condition is seen when the disease is disseminated.

Directions for making X-ray examinations with the fluorescent Screen.—The excursion of the diaphragm should be drawn on both sides of the chest in quiet breathing, in full inspiration, and in forced expiration. The lungs should be carefully observed, particularly the apices; if the disease is in the early stages, only one apex will probably be affected, and the

abnormal apex may be determined by comparing it with the normal. This comparison should be made both during inspiration and expiration, but the affected area will be more evident during full inspiration than expiration (see Fig. 25).

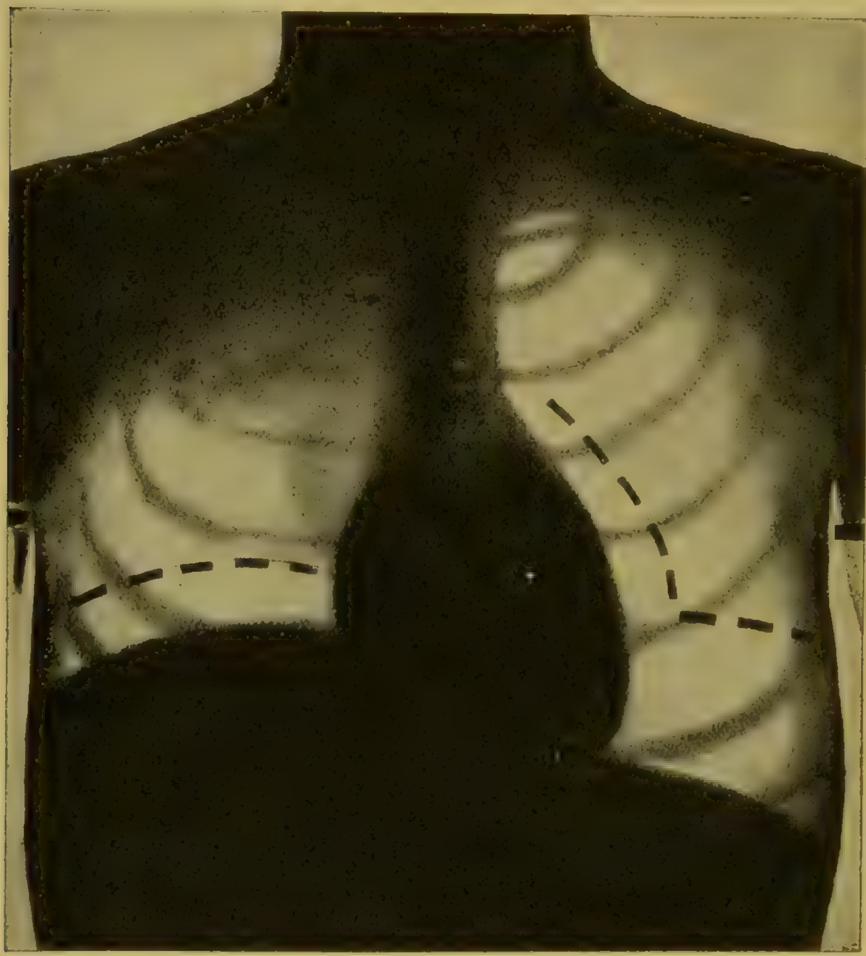

FIG. 24.—Diagram of pulmonary tuberculosis. Right side. Right apex darker, and excursion of diaphragm shorter than normal on right side. In the early stage the slight shadow cast is best detected at full inspiration. In this diagram the apex is darker, and the excursion of the diaphragm is more restricted than in the very early stage of the disease; partly for purposes of illustration, and, in the case of the apex, also because it is difficult to get a slight amount of shadow reproduced in the half-tone. The lines under the axillæ indicate the nipples. (From *The Roentgen Rays in Medicine and Surgery*.)

The light in the tube should be turned so low, by means of the adjustable multiple spark-gap (see page 474), that the fluorescent screen over the normal lung is scarcely illuminated, as the contrast between the diseased and the healthy areas is thus more apparent, and the differences in density between them which would be wholly overlooked with a bright light are obvious. If both apices are slightly diseased, the

physician must compare the brightness which he sees with the mental picture of what it should be for an individual of the given patient's build, for the lungs of very stout people would not normally appear so bright as those of thin persons. In the early stages of the disease, however, both apices are rarely, if ever, affected, and when both are involved the disease has generally progressed so far that it is very evident by other methods of examination. It is hardly necessary to say that before examining the chest the condition of the practitioner's eyes should be

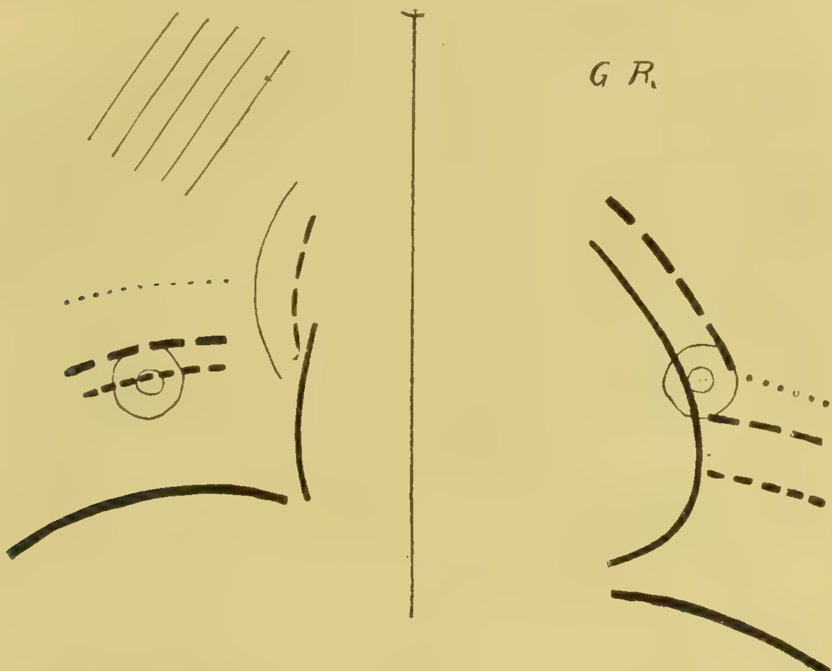

FIG. 25.—G. R.. Outlines taken from a case of very early tuberculosis. *Density*; darkened right apex. *Diaphragm lines*: The lowest full curved lines are the diaphragm lines in deep inspiration; the two broken lines above these, the lines in the inspiration and expiration of quiet breathing respectively; the dotted lines above these, the diaphragm lines in forced expiration. It will be seen that the excursion of the diaphragm in quiet breathing is shorter on the diseased than on the normal side, and that during expiration the diaphragm ascends higher than on the normal side. This X-ray tracing is given to indicate that we should study the movements of the diaphragm not only between expiration and deep inspiration, but also during quiet breathing and forced expiration (½ life size). (From author's work, *Roentgen Rays in Medicine and Surgery*.)

carefully tested by the spinthariscope, and that the examination should not be made until the scintillations in it are clearly visible.

A second X-ray examination, at least, should always be made after an interval of some days or, better, weeks, and if the appearances already observed still obtain, other indications of tuberculosis should be carefully looked for, especially an evening rise in temperature.

In cases of early pulmonary tuberculosis the screen, as a rule, gives better results in the hands of an experienced physician than the radiograph, but sometimes both are needed.

It is recognised that one of the best ways of diminishing the mortality

in pulmonary tuberculosis is to make an early diagnosis. In 1896 I directed attention to the assistance that X-rays may afford in this respect (67), and desire again to emphasise their special value in cases in which the disease is in such an early stage that the physical signs are not definite.

X-Rays as an aid in diagnosis.—An X-ray examination gives an early warning of a departure from the normal in the lung, and in connexion with the history makes it possible for the physician to make a diagnosis earlier in the disease in some cases than hitherto; but the diagnosis of tuberculosis is not made by the X-rays alone—for instance, the shaded apex and restricted excursion of the diaphragm might be due to recent pneumonia in the upper lobe; however, this point can be settled by a second X-ray examination made some time later. The X-ray examination is of assistance not only as an aid in diagnosis in cases in which there are no physical signs, or they are doubtful or slight, but also in cases in which an accompanying emphysema, bronchitis, pleurisy, or pneumonia might disguise the ordinary physical signs—for instance, emphysema would mask the dulness characteristic of dense tuberculous areas, but would present no obstacle to an appreciation of the increased density of the lungs when examined by the X-rays; in cases in which the physical signs indicate tuberculosis, which the X-rays do not confirm; in cases of tuberculosis of the bones or some other parts of the body, to ascertain if the lungs are also affected; in patients between fifteen and thirty years of age who have a tuberculous family history. Successive X-ray examinations are of value in showing that the disease is more extensive than the physical signs indicate, and in determining the progress of the disease in acute cases. By this means an otherwise unsuspected and rapid progress may be detected, and the prognosis and treatment of these cases in consequence greatly modified. For instance, the cruelty of sending a patient who is rapidly failing on a long and expensive journey in search of health might be avoided. X-ray examinations may also be of assistance in pointing out cavities in the lungs.

Pneumonia.—In pneumonia the affected lung or lungs cast a shadow on the screen, and the region often involved, when the process is not extensive, is that between the second and fourth ribs. The excursion of the diaphragm is restricted, and usually in its lower part, on one or both sides of the chest, because the lung or lungs are not able to expand to their normal extent, and also perhaps because of pleuritic adhesions; if the pneumonic process is extensive the diaphragm lines may be wholly obliterated on one or both sides of the chest. The heart is enlarged, especially on the right side, and if there is pneumonia of one lung only, is apt to be displaced. As the patient improves, the practitioner by making successive X-ray examinations can observe the gradual return of the heart to the normal, both in size and position, the lightening and diminution in extent of the dark areas in the lungs, and the increase in the excursion of the diaphragm as the lungs clear up. Fig. 26 illustrates the appearances seen on the fluorescent screen in pneumonia

on the seventeenth day of the disease when the physical signs had disappeared.

The methods of examination for this disease have already been indicated in the general directions given on pages 485-493, and in the special directions on page 493, and need not be further considered.

FIG. 26.—Diagram of pneumonia. Seventeenth day of disease. No physical signs on or after this day. Dark area and restricted movement of the diaphragm on the left side; the movement is also less than normal on the right side. The dark area diminished gradually, and the excursion of the diaphragm on both sides increased from week to week. There were still X-ray signs on thirty-second day. Nipple level indicated by heavy lines under axillæ. (From *The Roentgen Rays in Medicine and Surgery.*)

The X-ray examination enables the practitioner to determine the extent of the disease, whether or not it is limited to one lobe, or includes one lung and part of the other. For instance, by allowing the light to pass through the chest of one of my patients at an angle from the left front to the right back, it was evident that the disease was limited to the lower right lobe, as the outline of the lobe could be easily

traced. It likewise enables the practitioner to determine with greater accuracy when the lungs become normal, for the X-ray signs may be noted on the fluorescent screen when there are no longer any signs by auscultation and percussion. This shows that the X-rays are a more delicate test than the older method of examination.

The X-rays are also of assistance in making a diagnosis of pneumonia in cases in which the physical signs are obscure, as in some cases of pneumonia in old people, or in central pneumonia. For example, a child of eight years of age came under my care at the Boston City Hospital with no history. Two physicians examined her and found no physical signs in the chest, and I was inclined to accept their diagnosis of cerebro-spinal meningitis; but to obtain further information I made an X-ray examination with the screen, and finding that there was a dark area over one lobe, and a restricted excursion of the diaphragm on the same side, made the diagnosis of central pneumonia. This diagnosis was confirmed by a marked crisis and by the improvement of the lung, as shown by further X-ray examination. Auscultation and percussion gave no signs of pneumonia during the course of the disease.

Empyema after pneumonia may be overlooked, and appendicitis may be confounded with pneumonia, in the absence of X-ray examinations. These examinations also indicate by the appearance of the lungs in some cases of influenza that pneumonia is present, although no signs of this disease may be found by auscultation and percussion. A knowledge of the appearance of the lungs in pneumonia is of assistance in making a differential diagnosis between this and some other diseases, as, for instance, between pleurisy with effusion and pneumonia, or tuberculosis and pneumonia.

Emphysema.—In this disease (1) the pulmonary area appears brighter than normal on the fluorescent screen and more extensive; (2) the excursion of the diaphragm is restricted in the upper part of its normal movement, and is lower down in the thorax; (3) the heart changes its position very little between inspiration and expiration, and remains largely in the position of deep inspiration; its long axis is more nearly vertical than in health, and its right side is enlarged. The outline of the heart, which it is difficult and frequently impossible to obtain by auscultation and percussion, can be followed with great clearness on the fluorescent screen. The diagnosis of emphysema can be made by the X-ray examination alone, and in some cases this disease can be recognised by its aid when it has been overlooked by the physical signs, especially in young patients. Fig. 27 illustrates the appearances seen on the fluorescent screen in emphysema.

The physical signs of tuberculosis may be hidden by emphysema, as already mentioned, or may hide emphysema; but the X-rays reveal the signs of both diseases, the combination of which is not rare. If bronchitis and emphysema are associated the emphysema might be overlooked, as the bronchitis would diminish the brightness of the lungs, and the abnormal excursion of the diaphragm might be ascribed to the bronchitis

only; but a second X-ray examination, made after an interval, would be rightly interpreted if the bronchitis had meanwhile improved.

Pleurisy with Effusion.—In pleurisy with small effusion (1) the lower portion of the affected side is dark, and (2) the whole or a part of the diaphragm on this side, according to the extent of the disease, is obliterated

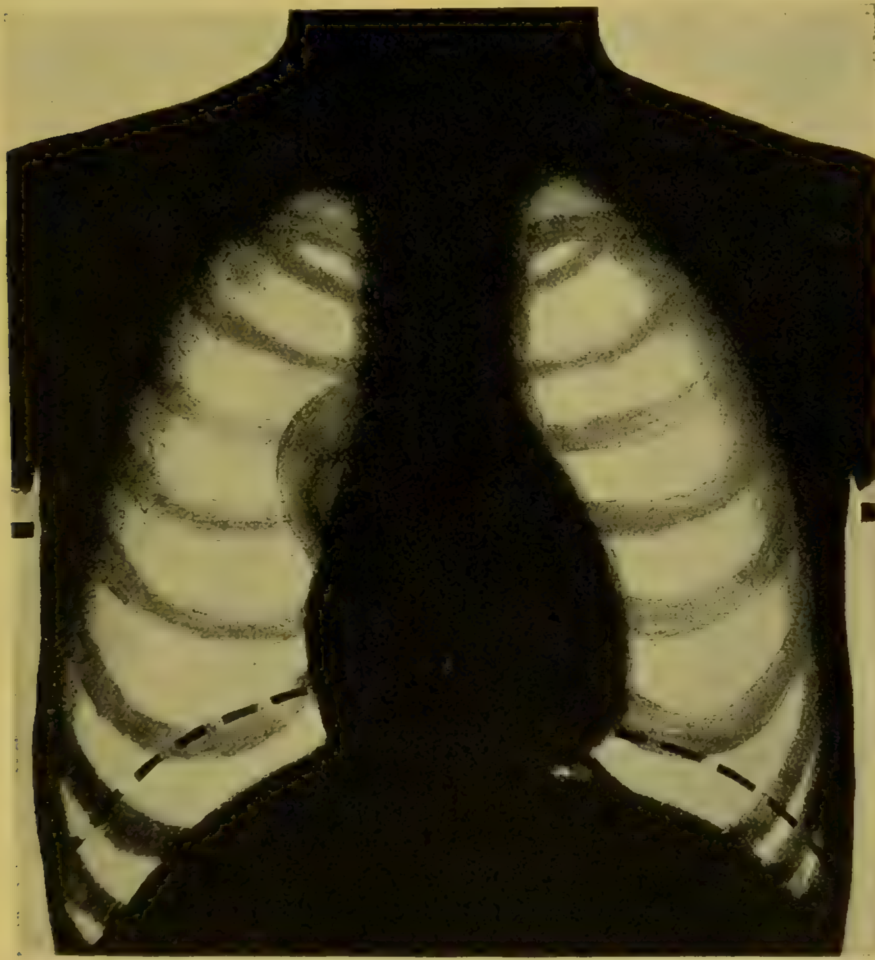

FIG. 27.—Diagram of emphysema of both lungs in full inspiration. Broken lines show position of diaphragm in expiration. Nipple level indicated by heavy lines under axillæ. Lungs brighter and long axis of heart more vertical than normal; right side of heart enlarged; excursion of diaphragm shorter than normal, and low down in the thorax. (From the author's work, *The Roentgen Rays in Medicine and Surgery*.)

(see Fig. 28). In pleurisy with large effusion the whole of the affected side is dark, the diaphragm and ribs are not visible, and the heart is much displaced.

In examining a patient who has pleurisy with effusion, the outline of the dark area, as well as the other outlines in the chest, may in most cases be seen to change when the patient alters his position. The patient should therefore be examined lying on his back, and in a sitting position,

and the outlines traced and compared. He should also be examined both when lying on his right and on his left side, the light going through the chest horizontally, with a view to distinguishing between a possible effusion in his chest and a dense lung.

The X-ray tracing in Fig. 29 shows that the dense area seen in the

FIG. 28.—Diagram of pleurisy with small effusion ; inspiration. Lower portion of right lung darkened by the effusion and diaphragm lines obliterated on this side. Broken lines on left side show position of heart and diaphragm in expiration. Heavy lines under axillæ indicate level of the nipples. (From the author's work, *The Roentgen Rays in Medicine and Surgery*.)

chest of the patient varied with his change of position, and therefore that it was due to fluid in the pleural sac and not to a dense lung. The patient was examined in a prone and a sitting position with the tube behind him and 70 centimetres distant from the screen and the anode opposite the point where the median line crosses a line joining the lower borders of the fourth ribs (the nipple line).

An X-ray examination is a more trustworthy method for determining

the presence of pleuritic effusion as indicated by a displaced heart than is percussion, especially if the heart is displaced to the right, and may indicate the presence of an encysted pleurisy or of an interlobar empyema or pleurisy more clearly than the physical signs. Emphysema associated with pleurisy is not always recognised by the physical examination, but it may be indicated by an X-ray examination. Pleurisy with effusion and tuberculosis are not seldom associated, but the latter disease might be overlooked in its early stage if an X-ray examination were not made after

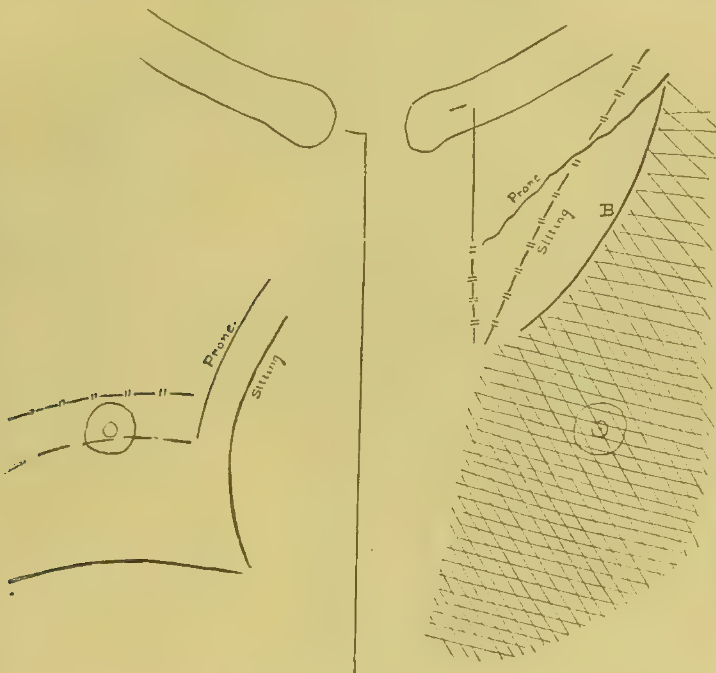

Fig. 29.—Pleurisy with effusion on the left side. The lines marked "prone" and "sitting" on the left side represent the height to which the fluid rose when the patient was examined in these respective positions; the line marked "B" the height to which it rose when the patient was examined in a sitting position with his left shoulder turned toward the observer. The lines "prone" and "sitting" on the right side, the border of the heart when the patient was lying and sitting respectively. In all these cases the observer was looking into the thorax from the front of the chest; the tube was behind the patient and 70 centimetres (27½ inches) distant from the screen. (From the author's work, *The Roentgen Rays in Medicine and Surgery.*)

the fluid had subsided. The X-rays also assist the practitioner in determining the presence of pleuritic adhesions.

Hydrothorax, Pneumothorax, Empyema with Permanent Opening, Pneumohydrothorax, Pyopneumothorax. — In hydrothorax the lower portions of the chest appear darker than normal on the fluorescent screen, and the outlines of the diaphragm are obliterated. If the disease is more extensive the darkened area extends upwards. In pneumothorax, on the contrary, the light area is brighter and larger than normal on the diseased side; the lung is retracted, the diaphragm has little or no movement, is low down in the chest, and the organs on the affected side are displaced to the

opposite side, the amount of displacement varying with the pressure of the air in the chest. The patient should be examined lying on his back on the stretcher (see Fig. 30).

In empyema with permanent opening the size of the darkened area varies with the amount of lung involved, the extent of the cavity, etc.

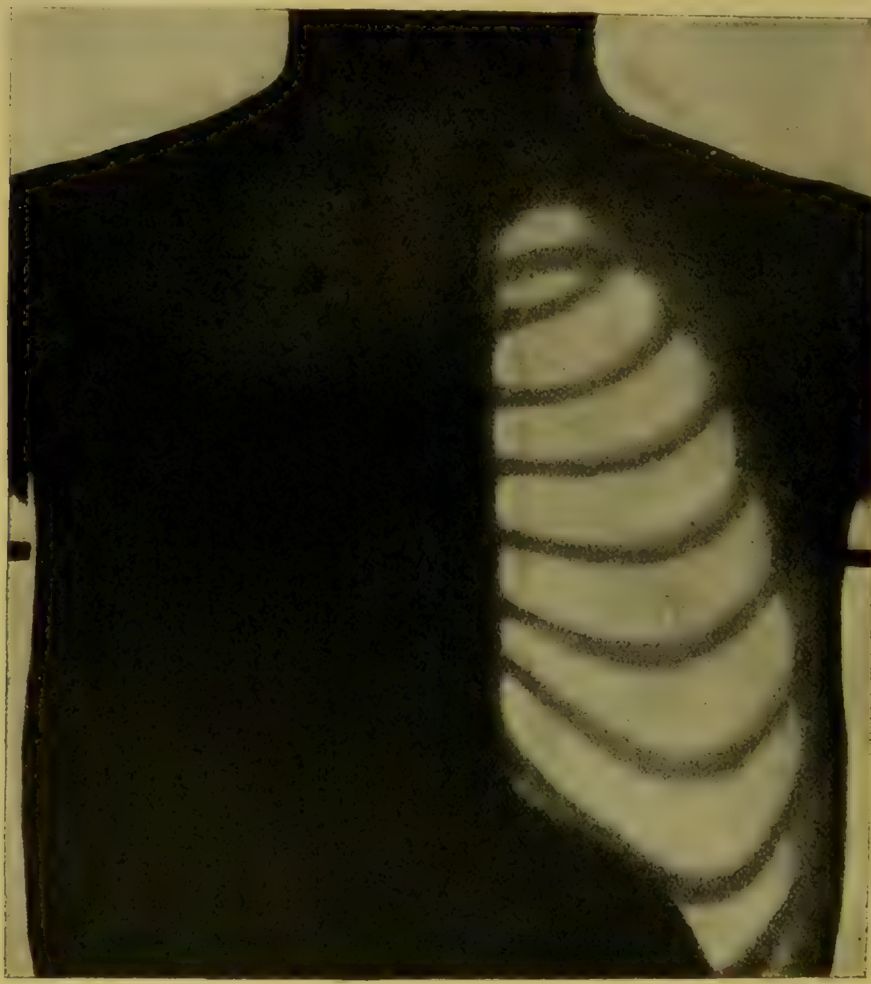

FIG. 30.—Diagram of pneumothorax on left side, and tuberculosis on right side. The diagram is too dark at the right apex. Left side brighter than normal and bright area more extensive. Diaphragm low down in chest; little or no movement. Organs on left side displaced to right. Heavy lines under axillæ indicate level of nipples. (From the author's work, *The Roentgen Rays in Medicine and Surgery.*)

Pneumohydrothorax or Pyopneumothorax.—When a patient affected with this disease is examined in a sitting position, with the tube behind him on a level with the fourth rib, the upper portion of the diseased side is seen to be abnormally light and the lower dark. In this upper portion toward the median line the shadow of the retracted lung may often be

seen. The heart is displaced to the opposite side, and when the fluid is at a suitable level the pulsations of this organ may be seen to disturb the surface of the fluid, especially if the pneumohydrothorax is on the left side. The general appearances in the diseased side resemble a tumbler partially filled with ink (see Fig. 31). If the patient is examined lying

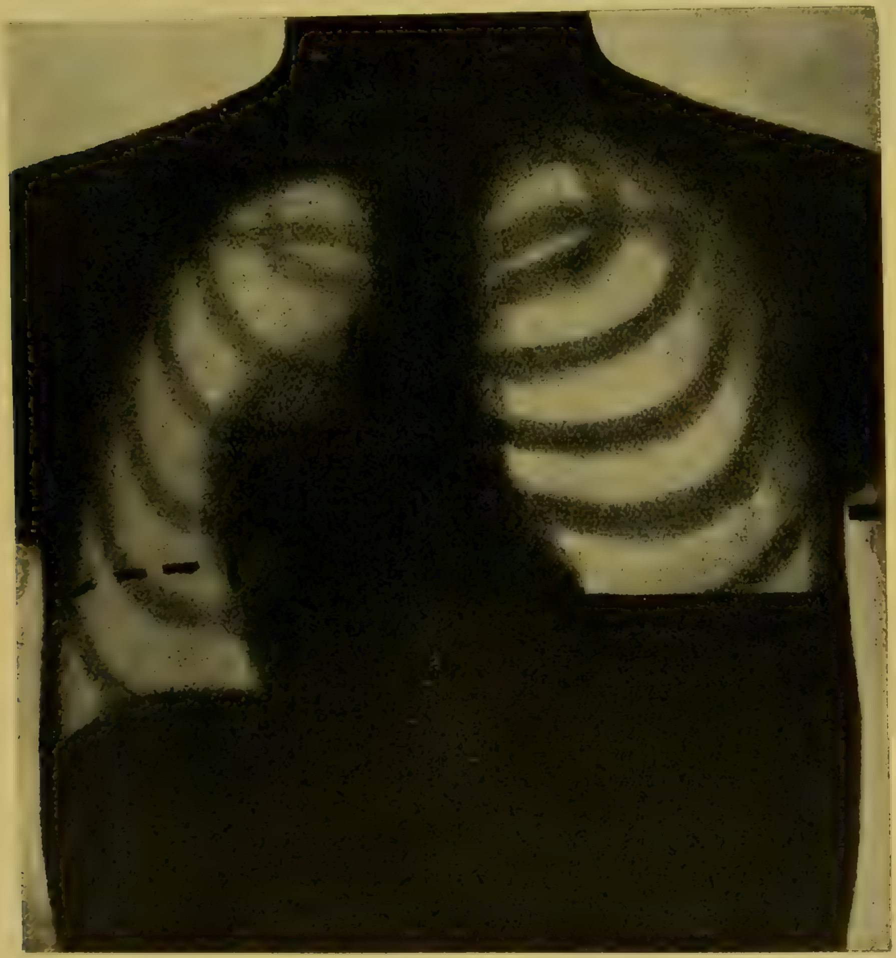

FIG. 31.—Diagram of pneumohydrothorax. Left side. Sitting position. Level line of fluid seen in left chest. Heart displaced to right. Retracted left lung not indicated; it would make a slight shadow in upper portion of left chest. Heavy lines under axillæ indicate level of the nipples. (From the author's work, *The Roentgen Rays in Medicine and Surgery*.)

on his back, with the tube below him, the whole of the affected side is dark, because the fluid flows over it.

During the past eight years I have been surprised to find patients with pneumopyo- and pneumohydro-thorax more frequently than ever before in my experience. This is doubtless due to the use of X-ray examinations. I have been struck with the amount of displacement of the heart which may take place in some of these cases owing to the pressure of the air in the chest.

Heart

The heart may be well seen by means of the fluoroscope, and its outlines, including much of the anterior, posterior, and lateral borders, may be observed; but these outlines may be in part wholly obscured if the pulmonary areas are not clear. The heart may be examined with the patient standing, sitting, or lying down. It can be seen better during full inspiration than during expiration. The horizontal diameter of the heart measured at full inspiration and at expiration will vary, because during the former period the axis of this organ is more vertical. The tube must

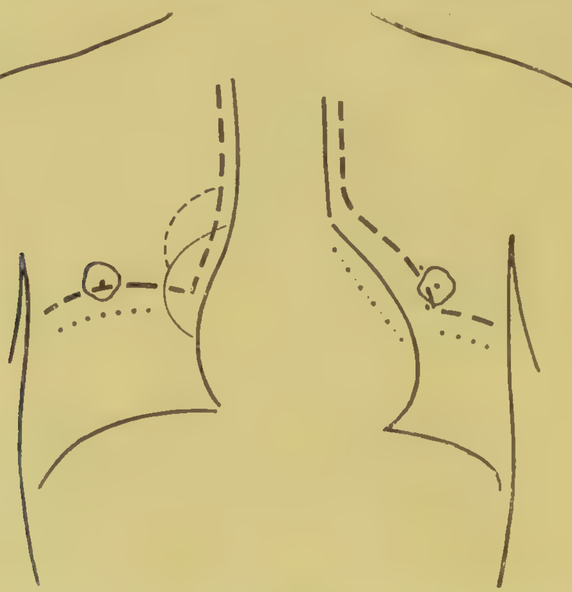

FIG. 32.—Diagram of heart movements representing the borders of the blood-vessels, heart, and diaphragm—the full lines in deep inspiration, the broken lines in expiration, the dotted lines just below the broken ones, the position of the diaphragm in ordinary inspiration. The line of large and small dots inside the left border of the heart shows the position of the left border in systole, the full line in diastole, during full inspiration. The other movements of the heart—namely, those of the apex, the right ventricle, and the right auricle—are not indicated in the diagram. (From the author's work, *The Roentgen Rays in Medicine and Surgery.*)

be in the proper position, and the outlines seen must be properly recorded or errors will result. Fig. 32 illustrates the movements of the normal heart when the patient is examined lying down.

If the heart is much enlarged its size can be more accurately determined by placing the tube under one border and drawing its outline on the skin, and then moving the tube under the other border and tracing its outline. To accomplish this, first obtain one border of the heart with the anode of the tube below the median line, then measure the horizontal distance from this border to the edge of the stretcher, and next move the tube until its anode is an equal distance from the plumb line held against the stretcher. This same method may be used if an accurate measurement of a large new growth, for instance, in the lung is desired.

The importance of knowing the size of the heart, as well as its position, need not be dwelt upon; but it is important to bear in mind that the size of hearts which are somewhat larger or smaller than normal often cannot be determined accurately by percussion. The fluoroscopic examination not only gives the size with greater accuracy, but it also gives fuller information. When the heart is displaced the error in

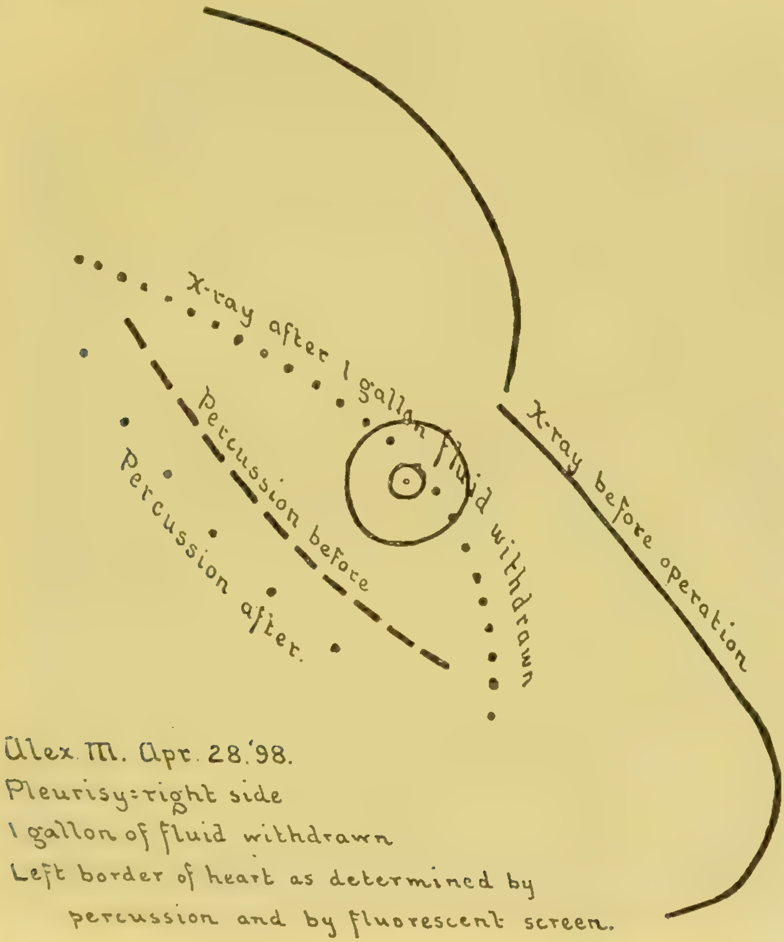

FIG. 33.—Right-sided pleurisy. Shows the difference in the position of the left border of the heart as determined by the X-rays and by percussion both before and after operation. One-third life size. (From the author's work, *The Roentgen Rays in Medicine and Surgery.*)

determining its border by percussion is often surprisingly great, especially in displacements to the right.

Causes of Displacement. Inaccuracy of Percussion.—The X-ray examination may show the causes of displacement very clearly. This displacement may be due to fluid or gas in the pleural cavity. The figure on this page illustrates this point. The full and dotted lines, obtained by means of the fluorescent screen, show the position of the left border of the

heart before and after the fluid was withdrawn respectively. The broken line and the dotted line parallel with it indicate the left border of the heart as shown by percussion before and after the fluid was withdrawn. The inaccuracy of percussion is illustrated by this case.

The displacement of the heart may be caused by contraction of pleural adhesions. In cases where the heart has been displaced by a pleuritic effusion, and remains fixed in this position after the effusion has been absorbed, the fluorescent screen will give a wonderfully accurate picture of the conditions present; it may indicate at what point the heart is held when it fails to move normally during deep inspiration. Under these conditions an enlarged heart might be indicated by the ordinary methods of examination. For example, the left border of the heart of one of my patients was outside the left nipple, and he had been told by several physicians that he had a seriously enlarged heart, but the fluoroscopic examination showed that the heart was normal in size, but was held in its unusual position by adhesions. As the patient was a professor who led a very quiet life, the anxiety that his heart would not serve his needs was easily relieved. It is essential to distinguish between a heart that has been drawn to the left and one that is enlarged to the left, and this distinction may be unusually well made by the aid of the fluoroscope. Again, in chlorosis, for example, the heart may appear by percussion to be enlarged both on the right and left sides, and as the patient improves seem to approach the normal, but the X-ray examination shows that this apparent decrease in size is really due to the descent of the diaphragm following the use of laxatives, and consequently to the change in the direction of the long axis of the heart. Displacement of the heart may be due to an unequal expansion of the lungs.

In making X-ray examinations of the thorax the shadow of the mediastinal contents should be noted with care, especially if the patient is examined in different positions and the respective outlines drawn on the skin are compared, as these contents are subject to instructive changes.

The fluorescent screen is of assistance in determining the presence or absence of dextrocardia. In one case of apparent dextrocardia that was brought to me for X-ray examination, the fluorescent screen showed that the heart was drawn to the right, probably as a result of a pleurisy five years before. A radiograph, taken before I saw the patient, had appeared to confirm the diagnosis of dextrocardia made by the history and physical examination.

The pulsations of the heart can be watched by means of the fluorescent screen in cases of irregular action; a differential diagnosis may often be made between an enlarged heart and a pericardial effusion, as the shape of the heart and the pulsations would not be the same in the two cases. If the triangle described on page 486 can be wholly seen by transverse illumination of the chest, pericardial effusion is not present to any extent. The effect of treatment can be watched by successive X-ray examinations in dilatation of the heart. X-ray examinations give warning of the serious

condition of a patient by showing the lack of efficient pulmonary circulation and presence of passive engorgement (see Fig. 34). They are also of value as they prompt precautions against unwise activity on the part of patients with serious disease.

Thoracic Aneurysms.—The appearances seen on the screen depend

FIG. 34.—Diagram of passive engorgement of the lungs from valvular disease. Heavy lines under axillæ indicate level of nipples. In valvular disease I have seen much darker lungs than the diagram indicates become clear, and the dyspnœa cease after treatment by digitalis. (From the author's work, *The Roentgen Rays in Medicine and Surgery.*)

upon the size and position of the aneurysm. Fig. 35 illustrates an aneurysm in the early stage.

The patient should be examined, in a revolving chair, by means of the screen, from both the back and the front of his chest, and from side to side if he is well enough; if not, in a prone position. An X-ray photograph may also be serviceable. A diagnosis of thoracic aneurysm may be made by the X-rays alone before there are physical signs, a

conclusion of great value, as treatment in the early stage of the disease is most efficacious in prolonging life. The extent of an aneurysm can also be well determined by an X-ray examination. Further, patients may be assured that no aneurysm is present, although physical signs

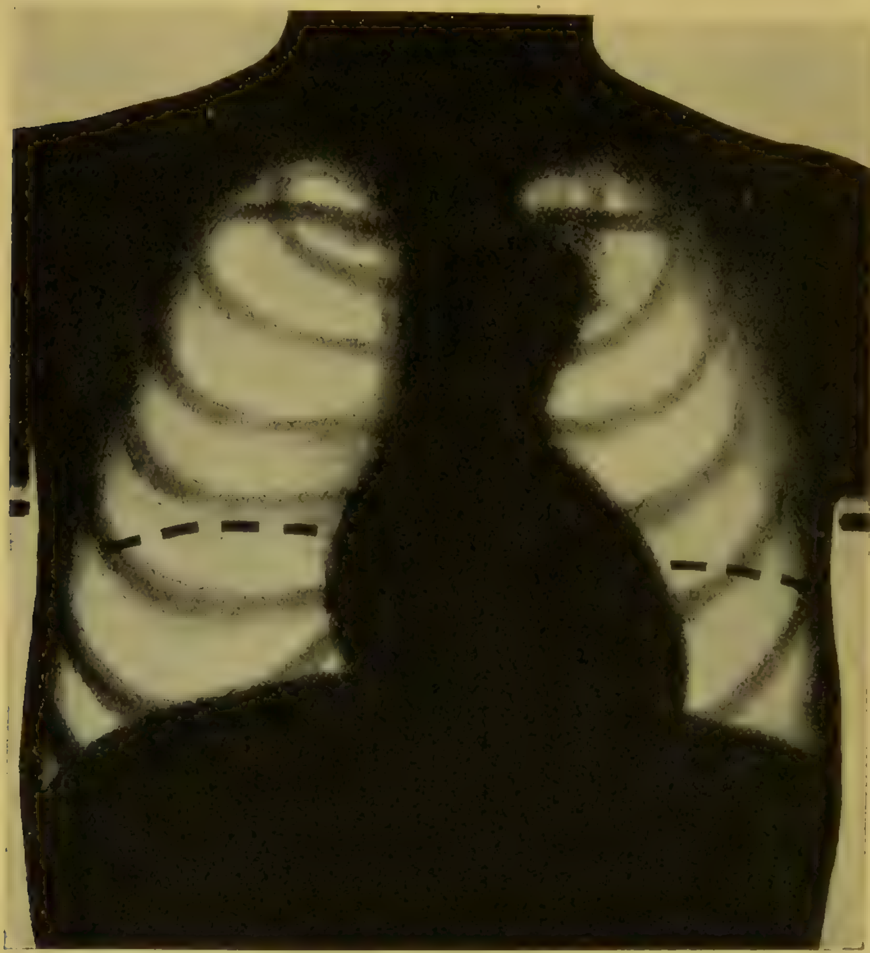

FIG. 35.—Diagram of an aneurysm of the descending aorta. Full inspiration. The aneurysm would often be higher in the chest than is shown in this diagram. A dilatation of the ascending arch of the aorta would usually cast a shadow on the right side of the sternum. Broken lines show position of diaphragm in expiration. The heavy lines under the axillæ indicate the level of the nipples. (From the author's work, *The Roentgen Rays in Medicine and Surgery*.)

have led their medical attendants to fear that the disease existed. For example, I recently saw a patient who was thought to have a thoracic aneurysm. The X-ray examination showed that he had an enlarged heart and a passive congestion of the lungs, the appearances seen in the chest being similar to those indicated in Fig. 34. The administration of digitalis was followed by marked improvement.

Out of thirty-seven cases which I examined some years ago for

suspected aneurysm by means of the X-rays, sixteen showed normal outlines, two had more or less dilatation of the aortic arch, and nineteen had typical aneurysms, seventeen of which were in the arch of the aorta. The seventeenth case had also an aneurysm of the innominate artery, the eighteenth case aneurysms of the innominate and of the subclavian artery respectively, and the nineteenth case an aneurysm of the subclavian artery. There were no physical signs in nine of these nineteen cases. A later group of cases confirms this experience.

Intra-Thoracic new Growths.—The X-rays are of use in determining the presence of new growths and enlarged glands in the chest. The patient should be examined with the X-rays going through the body from different directions, and the result of these examinations should be considered in connexion with the history of the patient and other points.

The X-rays are also of value not only in making a diagnosis of abscess of the lung, but also in locating the site of the pus, thus indicating the most favourable point for operation and determining the extent. They likewise indicate the presence of echinococcus cysts in the lung and the presence of chronic interstitial pneumonia; in the latter condition the mediastinum is displaced towards the affected side.

The X-rays can be employed with advantage in the examination of candidates for life insurance. There is no method that gives more trustworthy and complete evidence of the normal or abnormal condition of the organs in the chest than a careful examination with the fluorescent screen, made by a physician who is experienced in its use.

Œsophagus.—The position of a stricture of the œsophagus may be determined by the X-rays by the insertion of a rubber tube closed at one end and filled with shot or mercury, and a diverticulum may also be recognised, if its position is favourable, by mixing bismuth with the food, as this would lodge in the diverticulum and the bismuth would cast a shadow.

In concluding this brief account of the place of X-ray examinations in diseases of the chest, I should add that in examining the thorax the condition of one organ must not be considered alone, but in connexion with other outlines in the chest; that these examinations should be made by trained physicians, preferably by specialists of thoracic diseases; thirdly, that in unusual cases the physical examination of the chest is not complete unless an X-ray examination is also made.

The writings of Béclère and of Holzknecht, the atlas of Weinberger, and the plates of v. Ziemssen and Rieder, will be of special value to those who desire to make a study of the use of the X-rays in diseases of the thorax.

Abdomen

The thorax is extremely well suited for examination by the X-rays, because the lungs are so largely filled with air (which is easily penetrated by the rays) that the contrast between them and a dense organ,

such as the heart, is very marked. In the abdomen, however, such contrasts do not as a rule prevail, although at times there is so much gas in the large intestine that its position may be recognised.

Methods of Examination.—When the practitioner desires to examine the stomach, the patient should have a good movement of the bowels the day before and the morning on which the observations are to be made; the stomach should be free from food, and when everything is in readiness he should take food, such as bread and milk, mixed with an ounce of subnitrate of bismuth. The size, position, and shape of the stomach may then be observed during digestion by making successive X-ray examinations. The digestive tract may also be observed by giving the patient capsules coated with celluloid to prevent them from dissolving, and filled with bismuth to enable them to cast a shadow on the screen. These methods are adapted only to young or very thin patients.

(*a*) *Introduction of Air or Gas.*—Air or gas may be introduced into the hollow organs of the abdomen in order to obtain information as to their position and outline; or air or gas may be introduced to displace the parts near the special organ to be studied, in order that its shadow may stand out against the light area thus produced. For instance, under some circumstances the large intestine may be distended with advantage by pumping air into it by a syringe; or the stomach may be distended by administering the two ingredients of a Seidlitz powder separately.

(*b*) *Pressure of Air from Outside.*—Another method that I have found useful in examining the abdomen is the displacement of some of the abdominal contents by the pressure of air on the outside of the body. The patient is placed on his back with the photographic plate under him and the tube above him. A bag of pure rubber, such as is used to distend footballs, with a tube closed with the simple valve used on bicycle tires, is placed over the abdomen, and is held in position by a broad band of cotton cloth provided with straps and buckles, or a towel pinned tightly around the abdomen. Then by means of a small bicycle hand-pump the bag is distended, and the pressure thus brought to bear on the abdominal contents diminishes the thickness through which the rays must pass to the photographic plate and a better radiograph therefore results. This method is the one I always use when taking a radiograph of the kidneys (or of the lower part of the spine), and is especially useful in stout patients (see p. 482).

In renal disease X-ray examinations of the abdomen are of service by showing the size and position of the kidneys, by indicating a floating kidney, and by showing the presence of calculi (this latter subject has been already touched upon under the surgical uses of the X-rays); they are also valuable for determining the presence of ascitic fluid, and for pointing out a phantom tumour, as, if the suspected tumour is caused by gas, a bright area would be seen on the screen, and the diagnosis of a new growth might be excluded. They likewise enable the practitioner to recognise new growths, but only at a late stage; to follow the

lower outline of the liver in children, and in some grown people under certain conditions; and to observe changes in the outline of the liver and an enlarged liver, if these changes affect the diaphragm; and to recognise the lower border of the spleen, the large intestine being distended with air.

Subdiaphragmatic Abscess.—Certain conditions seen by means of the X-rays may call the attention of the practitioner to the correct diagnosis in obscure cases. The following case illustrates this point (see Fig. 36). The diaphragm on the right side was pushed high up in the thorax, and below it was a light area (gas), and under this a dark tract (fluid). When the patient bent from side to side the line marking the top of the dark shadow remained level, but it became wavy when he was gently shaken. These appearances indicated that the dark shadow

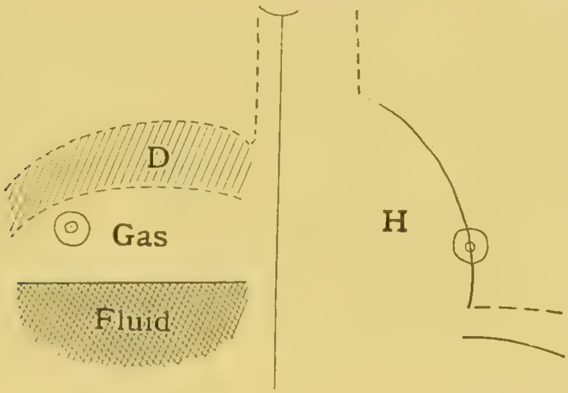

FIG. 36.—Subdiaphragmatic abscess. September 24, 1902. X-ray examination with patient in a sitting position. Tube behind the back and fluorescent screen on front of chest. D, right diaphragm; H, heart. Horizontal line marking the top of the fluid remained level when the patient bent from side to side, and became wavy when he was gently shaken. (From the author's work, *The Roentgen Rays in Medicine and Surgery*, 3rd ed.)

was caused by fluid and the light space above it by gas. By means of these observations the correct diagnosis of subdiaphragmatic abscess was made. The operation confirmed my X-ray examination in every respect.

The pelvis may be studied by means of radiographs. In order to obtain an accurate measurement the tube should be placed at a considerable distance from the photographic plate, as it is not possible to bring the plate close to the pelvis. If a very precise measurement of the transverse diameter of the pelvis is desired, first one-half may be radiographed and then the other, by placing the tube over the outer edge of the brim of each side of the pelvis respectively. In the unusual cases of deformed pelvis radiographs can give much and definite information.

Turbert reported a case in 1898 in which the X-rays confirmed the diagnosis of extra-uterine pregnancy. Varnier and Pinaud have observed the gravid uterus, and have found that after five months the posterior wall of the pelvis and the vertebral column are hidden.

Therapeutic Uses

The X-rays are of service as a therapeutic agent—(1) for treating certain diseases of the skin, (2) and of the glands and lymphatics, (3) for treating new growths, and (4) as an analgesic. They are not valuable as a germicide.

The chemical changes caused by the X-rays and the rays from radium are familiar to us in the radiograph and in the discoloration of glass, on and below the surface, through which the rays have passed for a long time. It is possible that the beneficent action of the X-rays and of the rays from radium in the treatment of disease is also due to the chemical changes they set up or to ionisation. The X-rays have the power, however, not only to cure, but also, as is well known, to produce serious injuries if not prevented by suitable precautions from reaching areas, either of the practitioner or the patient, other than those where they are needed; and if they are not given in the proper amount and of the proper quality.

X-Ray Dermatitis.—The acute dermatitis caused by the X-rays has been described by Kienböck as of four degrees: the first appearing after a latent period of twelve to sixteen days, and the second after a shorter latent period; in the third degree blisters, or even extensive exfoliation take place, the hair does not grow again, and there is atrophy of the cutis and papillæ; in the fourth degree an ulcer appears, which may not heal for some months or a year. Kienböck also describes three degrees of chronic X-ray dermatitis, the result of many X-ray exposures, differing in the seriousness of the effects they produce.

Differences in Tubes.—Tubes vary in the output of rays, and the same tube differs at different times. Some tubes give out four times as much light as others, or even more; therefore if the proper exposure in the first case were twenty minutes, in the second case it should be only five minutes. Otherwise, a powerful remedy has been used without determining the dosage. Given these conditions, it is not surprising that patients have been burned; the wonder is that more have not received injuries. But if X-rays of known quality and in measured amount are used, the danger from burns will be practically removed. Benoist has devised a radiochrometer for determining the quality of the rays given off by a tube, and Holzknecht a chromoradiometer for measuring the quantity of rays that reach the body and are absorbed in a given time. The method I now use is described below.

Method of Treatment; Length of Exposure.—The length of exposure depends on the amount and quality of the light, on the place of the disease—whether it is superficial or deep seated—and on the character of the disease. It is well to have the tube as a rule at a uniform distance from the patient in order to reduce the number of factors to be taken into consideration in determining the exposure, and to vary the exposure in

accordance with the amount of light of the desired kind that is allowed to reach the patient and the character of the disease.

Two Sets of Tubes; Quality of Light.—Two sets of tubes are desirable for therapeutic purposes; one set (tubes of low resistance) emitting a large proportion of rays of low penetrating power that are absorbed near the surface, and the other set (tubes of high resistance) a large proportion of rays of high penetrating power. Tubes should be chosen to suit the seat of the disease. If it be on or near the surface, a tube that is giving off a large proportion of easily absorbed rays should be employed; if the disease is deep seated, a tube giving off a large amount of more penetrating rays should be used.

Superficial Diseases.—(*a*) *General rule for length and frequency of exposure and distance of tube.*—It may be said, as a general rule for the treatment of superficial diseases, that the exposures should be of five minutes' duration for the first few sittings, and then be increased if necessary; that they should be given two or three times a week, and that the tube should be at the distance of 10 or 15 centimetres (6 or 8 inches). If a large area is affected the distance of the tube should be somewhat increased and the exposure lengthened in suitable proportion.

(*b*) *Method for carrying out an X-ray prescription and for obtaining the same dosage at different sittings.*—Suppose the practitioner gives his assistant the following prescription for a case of eczema:—

℞ X-light, for absorption in the skin, to the amount of 200 with the tube at a distance of 15 centimetres (8 inches) and an exposure of five minutes.

To carry out this prescription the assistant first takes the fluorometer reading (for method of obtaining reading and need of using the same fluorometer see page 477, and note) of one of his low tubes. Let us suppose that it is 24 inches. The square of this figure, namely, 576, expresses the total amount of light given out by the tube. He next determines the proportion of rays that would be absorbed in the skin by interposing an aluminium plate $\frac{2}{5}$ millimetre ($\frac{1}{64}$ inch) thick between the tube and the fluorometer (see next paragraph). Let us suppose that after the interposition of this plate the fluorometer reading is 18 inches. The square of this figure, namely, 324, represents the proportion of rays that penetrate the aluminium plate. Consequently the proportion that would be absorbed by the skin is the difference between 576 and 324, namely, 252. The proportion of rays emitted by this tube that would be absorbed by the skin being one-fifth more than the prescription calls for when an exposure of five minutes is given, the assistant reduces the length of exposure one-fifth, and gives an exposure of four instead of five minutes. The aluminium plate used to determine the amount of light that will be absorbed by the skin is of course removed before making the exposure. By the use of this method the same dosage can always be given if desired, whatever tube is used. It is convenient to have a table at hand which gives the squares of the usual fluorometer readings. The effect

produced by the highly penetrating rays of a low tube in passing through the skin may be neglected when determining the length of exposure necessary in superficial diseases.

Deep-seated Diseases.—*Exclusion of rays absorbed on or near the surface.*—In treating deep-seated diseases it is important that the rays of low penetrating power should be excluded in order that the length of exposure necessary to affect the diseased tissues below the surface may be given without burning the skin by the rays that are easily absorbed. To accomplish this end, I interpose between the tube and the patient different thicknesses of aluminium plates, corresponding in their power of absorption to the depth and character of the tissues intervening between the surface and the diseased tissue. The thickness of the aluminium plates required in these cases was tested in the following way:—I placed a series of aluminium plates of different thicknesses over an enclosed photographic plate, and beside them a piece of fresh skin 3 millimetres ($\frac{1}{8}$ inch) thick, and a piece of breast $1\frac{1}{4}$ centimetre ($\frac{1}{2}$ inch) thick that had just been removed, and took a radiograph of them. The result showed that an aluminium plate about $\frac{2}{5}$ millimetre ($\frac{1}{64}$ inch) thick would absorb rays of about the same power of penetration as the skin 3 millimetres ($\frac{1}{8}$ inch) thick, and that an aluminium plate $1\frac{1}{2}$ millimetre ($\frac{1}{16}$ inch) thick would absorb rays of about the same power of penetration as fatty tissue $1\frac{1}{4}$ centimetre ($\frac{1}{2}$ inch) thick. The practical application is simple. If a deep-seated disease is to be treated, an aluminium plate of such a thickness that it will absorb most of the rays which would otherwise be absorbed by the tissues intervening between the surface and the site of the disease, should be interposed between the tube and the patient. By the use of this method the length of exposure necessary for a deep-seated disease may be given without fear of burning the skin meanwhile by the rays of low penetrating power.

Method for obtaining the proportion of Rays suitable for treating deep-seated diseases emitted by a given Tube.—The square of the fluorometer reading (for method of obtaining reading see page 477) taken after the interposition of an aluminium plate between the tube and the screen of the fluorometer expresses the amount of light emitted by a given tube of sufficient power to penetrate below the skin. For instance, if the total amount of light issuing from a given tube of high resistance, as determined by squaring the first fluorometer reading, is 3600, that is, the reading taken before the interposition of an aluminium plate, and the square of the second fluorometer reading, taken after the interposition of the aluminium plate, is 900, this figure represents the amount of rays that is sufficiently penetrating to pass through the aluminium plate and strike the screen of the fluorometer, and, therefore, that is able to penetrate below the skin when that is exposed to the light instead of the fluorometer. In treating deep-seated diseases, as already stated, the aluminium plate remains in front of the tube while the exposures are being made to absorb the rays of low penetrating power that might otherwise burn the skin. The same fluorometer (see page 477, note) must

be used in order to obtain the same dosage at different sittings. The amount of suitable light, the distance of the tube, and the length of exposure appropriate for a given deep-seated disease being determined, the dosage can be repeated at another sitting by increasing or decreasing the length of exposure according as the amount of penetrating rays emitted by the tube used falls below or rises above the amount previously employed. The amount of light necessary is not the same for all deep-seated diseases. For instance, sarcomas require less than carcinomas.

Frequency of Exposure ; Character of the Disease.—In certain diseases, for instance, sarcoma, including those deeply seated, and Hodgkin's disease, treatment should be given at longer intervals than in other growths, because symptoms of toxæmia may follow a too energetic use of the rays, due to the large amount of the products of decomposition set free at one time into the circulation by the action of the rays on the diseased tissues ; though if opportunities for drainage exist less absorption will take place.

Quality of Reaction desirable when treating Diseases by the X-rays.—Practitioners differ as to the amount of reaction most desirable ; some believe in using the X-rays so vigorously as to produce a slight dermatitis, but this is not necessary.

Treatment by Medical Men.—The reprehensible custom has prevailed in some clinics of allowing X-ray treatment to be carried out entirely by nurses or non-professional men ; this should not be countenanced ; the best results can only be obtained when nurses or house officers, as well as the patients, are under the constant and direct supervision of a medical man of experience and judgment.

X-rays as an Analgesic.—The X-rays are useful as an analgesic, and have been employed to advantage for this purpose in some cases of neuralgia, of chronic rheumatoid arthritis, varicose ulcers, cancer, and other diseases.

The X-rays have also been used to advantage in tuberculous sinuses and in old or indolent ulcerations, and good results are reported in chronic tuberculous peritonitis. The X-rays are of service in warts, in deep and superficial scar tissue, corns, etc.

Glands and Lymphatics.—The X-rays have brought about some good results in goitre ; they have been used to reduce the spleen and glands in Hodgkin's disease, to act on the testes to produce at least temporary sterility, and on the enlarged prostate with probably some success. The X-rays cause the glands to diminish in size in adenitis, especially tuberculous adenitis in the neck. I have seen excellent results in these last cases, and think the X-rays should certainly be given a trial, as no harm will result from the delay of operative treatment which produces an unsightly scar.

Skin Diseases.—The X-rays are a very valuable remedy in psoriasis ; in some most obstinate cases they give prompt relief, and although the disease may return it does not always do so. For example, no recurrence has taken place in one of my patients who had suffered from psoriasis

of the whole body and extremities for forty years before treatment by the X-rays. In some cases of eczema the X-rays have proved themselves to be an excellent therapeutic agent; but it may be necessary to supplement this treatment with care in diet and rest. In acne vulgaris and acne rosacea gratifying results have been obtained, as well as in herpes zoster, sycosis, and favus. The X-rays do not kill the parasites in the two latter diseases, but they remove the hair which has become a source of irritation.

The treatment of lupus by the X-rays produces fair results. The method so successfully and devotedly pursued by Finsen is not applicable to all parts, notably the mucous membranes, and, according to Finsen, some portion of the mucous membrane is involved in 75 per cent of the cases, and these cases would therefore be, in part at least, accessible to the X-rays. The Finsen method is uncomfortable in the carrying out, and is usually followed by blisters. There are recurrences after all methods.

Healthy but superfluous hair can be removed by the X-rays, but this method of treatment has some dangers except in careful hands; the growth of hair may indeed be stimulated. Some good results have been obtained in nævus flammeus, in cutaneous blastomycosis, mycosis fungoides, tinea tonsurans, and pruritus. I have had good results in dermatitis herpetiformis.

New Growths.—Of the various diseases treated by the X-rays, superficial new growths have attracted the most attention, and there is now no doubt that the results obtained in many of these cases are not only temporarily good, but are also thus far permanent. The cosmetic results are excellent. My early cases were treated four years ago, and some of these patients are still well. No photographs are given for the reason mentioned on page 473. If recurrence does take place, prompt treatment by the X-rays for a short time is generally sufficient to cause the growth again to disappear. Furthermore, certain situations, such as the eyelids, which are not always accessible to operation, are easily treated by the X-rays. The X-rays seem likely to prove the best method of treatment in most superficial malignant diseases, if the cases are taken in the very early stages, and the treatment is given by a practitioner who knows how to use the method to the best advantage. Surgical interference in these cases is sometimes followed by a recurrence even more active than the original trouble. For example, a man sixty-one years of age, who had a small epithelioma of the lip, was operated on at the Boston City Hospital by an unusually experienced surgeon, but a recurrence took place in seventeen days. A second operation, even more radical than the first, the parts included extending below the chin to the neck, was then done, and was followed in about the same time as before by an extensive recurrence. When I saw the patient the area involved was a large part of the lower lip, most of the chin, and a tract below the chin running toward the neck. I began treatment by the X-rays directly, and improvement was steady and

continuous. Two years have elapsed since that time, and the man has been at work every day ; the only indication of the disease remaining is the scar on the chin and the puckering of the skin under the chin, which are the result of the operation. The masses of induration have

FIG. 87.—A. D., twelve years of age. Microscopical diagnosis, lymphosarcoma and round-celled sarcoma. Duration, seven years. Two operations. Before treatment by the X-rays. (From the author's work, *The Roentgen Rays in Medicine and Surgery*.)

disappeared. A second patient, a child six years of age, who had a spindle-celled sarcoma of the arm, was operated on twice, the recurrence taking place each time in about three months. I then used the X-rays, and he has now been well for three years.

Sarcomas, including those deeply seated, should be treated by the X-rays alone or after operation, according to the condition of the case.

Treatment, as already mentioned on page 515, should be given at longer intervals in cases of sarcomas than in other growths. Figs. 37

Fig. 38.—A. D., twelve years of age. After treatment by the X-rays. (From the author's work, *The Roentgen Rays in Medicine and Surgery*.)

and 38, made from photographs of a patient with lymphosarcoma, taken before and after treatment, show the good results that may be obtained, temporarily at least, by the use of the X-rays. The patient had under-

gone two extensive operations previously. When she came to me, not only were the glands in the neck enlarged, as shown in Fig. 37, but also those in the axillæ, the groins, and the thorax, and the spleen was enormously increased in size. The patient was weak and listless at the beginning of treatment, but became bright and active after this method had been used three or four weeks. The greatly enlarged glands of the neck were reduced as time went on to an almost normal size, the conditions in the thorax improved, and the very large spleen was markedly diminished. The relief, however, was not lasting, as there was a recurrence, and the patient died two years later. This case is referred to in part to show that the X-rays act below the surface.

Cases of sarcoma, which apparently recover, should be kept under observation and be treated from time to time to prevent the recurrence that might otherwise occur.

The effect of treatment by the X-rays in *Hodgkin's disease* is at first wonderful, but at present I believe this method is only palliative. Treatment must be given at longer intervals than is usual, as in the case of sarcoma and for the same reason.

Rodent ulcers have been successfully treated by the X-rays by Dr. J. H. Sequeira and others. Good results have also been obtained in cheloid.

Cancer of the Breast.—What shall we do when carcinoma of the breast is just beginning? Advise early operation, followed by X-ray treatment, to prevent recurrence, until we have a better knowledge of the limitations of the X-ray method. I add this qualification because when I contemplate the frequency of recurrence after operation, and the readiness with which the X-rays, when used in these cases, keep the disease at bay for considerable periods, in some instances for two years at least (the patients I have in mind are still apparently in good health), it is possible that the X-rays may be found capable of comparing very favourably with surgery. Further, in view of the surprising improvement, relief, and prolongation of life following the use of the X-rays in extensive and inoperable cases, and of the small proportion of cases, according to some estimates, that remain well for five years after operation, we should keep in mind the question of the treatment of malignant disease of the breast in the very early stage by X-rays alone. I have used the X-rays simply as a palliative in patients with extensive recurrence following removal of the breast, who have been so helped by this treatment as to be about and able to enjoy life for more than a year, and there is every present prospect that this condition will be further continued. This statement applies to patients who, when I saw them, seemed to be within a few weeks only of a fatal termination. Such favourable results are at present the exception, but with further knowledge and improved methods they may become more common.

In a few cases in which the disease, though not in the early stages, was eminently suitable for operation, and for which operation was strongly urged but persistently declined, I have thus far had satisfactory results from the use of the X-rays; the patients are in better general health than

they were at the beginning of treatment two years ago, and the induration which affected the greater portion of the breast is in large part gone. For example, a patient, who came to me two years ago with an irregular induration involving about two-thirds of the breast and a nipple very much retracted, declined absolutely to have an operation, and chose treatment by the X-rays against all medical and surgical advice. This patient is better now than she was two years ago—most of the mass in the breast has disappeared—and she has outlived some of her friends who, during this time, were suffering from apparently the same disease, but submitted to operation.

But I believe that we should not place all cancers of the breast in one group. There are some kinds that yield more readily than others to surgical measures, and there may also be some kinds that respond more readily than others to treatment by the X-rays. Further, some kinds may be helped more by operation and others by the X-rays.

Metastases.—The X-rays, as a rule, hold the disease in check, but they do not prevent metastases. We have yet to learn whether metastases are more likely to occur after operation, which necessitates division of the lymphatic and blood vessels, or after X-ray treatment. If it can be shown that metastases occur less often when the breast and neighbouring glands are treated in the very early stage of the disease by the X-rays, this method would have a great advantage.

The two methods of dealing with cancer of the breast are operation and the X-rays. The question may be fairly asked, though it cannot be answered for several years, whether some cases of carcinoma of the breast will not live quite as long if treated by the X-rays as if operated on; that is admitting, of course, that only a certain percentage can recover by either method. Surgical reports vary as to the percentage of recoveries and the duration of life after operation. On the other hand, the period during which the X-rays have been used for this disease is too short to justify a definite estimate of their value in this direction, especially as their use has been tentative. Neither has sufficient time elapsed to determine with precision the comparative value of the two methods when used in the early stages of the disease, but as patients would come earlier for X-ray treatment than for operation, the X-rays for this reason would have a decided advantage. Many patients conceal cancer of the breast, through fear of an operation, until it is too late; but as treatment by the X-rays is painless this method would attract such patients, and thus many might learn to seek relief in the earliest stage of the disease, when there is the greatest chance of recovery.

The X-rays may also give relief from pain, and in the hopeless cases give mental comfort, shorten the period of despair, and in some instances prolong life.

It is, I think, obvious that we may expect more success (*a*) when we can measure the dose, and (*b*) when we can apply the kind of rays adapted to the deep-seated diseases by eliminating from the combined

remedies the one that is harmful in these cases, and thus be able to use the suitable one in proper amount without the risk of injury from the other.

Leukæmia.—Treatment by the X-rays seems to reduce the size of the spleen and the number of leucocytes in cases of leukæmia, but Drs. Joseph A. Capps and Joseph F. Smith conclude from eleven cases reported by different practitioners, themselves among the number, that death may take place when the spleen is smallest and the leucocyte count normal; that X-ray treatment holds the disease in abeyance, but is not curative, although it is as yet too soon to say that the persistent treatment of an early case may not produce permanent results.

Radium.—The keen interest which has been aroused in radium, the similarity of its action to that of the X-rays as a therapeutic agent, and the fact that the two may sometimes be used to supplement each other, make it desirable to add a word in regard to it. Rollins was the first person, so far as I am aware, to perceive that radium salts would probably be of value in the treatment of disease. In the summer of 1903 I saw the successful work being done by Dr. Mackenzie Davidson in London and the work begun in Vienna by Holzknecht. Since that time I have treated fifty-one cases of new growths and twenty cases of skin diseases with radium, using 50 milligrammes of pure radium bromide.

Method of Treatment.—The radium, enclosed in a metal box with a thin mica cover, over which a thin rubber finger-cover is drawn, is placed on the part to be treated; a new cover is used for each patient.

Exposures; General Rule.—In treating superficial lesions, when 50 milligrammes of pure radium bromide are used, the exposures should be of one to four minutes' duration, and should be given once or twice a week.

Radium, like the X-rays, may produce a burn that does not manifest itself immediately. For my own protection I have had the capsule containing the radium set into a metal box, and have had attached to the box a flexible handle 30 centimetres (12 inches) long, in order to hold it at a distance when treating patients.

Radium, unlike the X-rays, is not of service in diagnosis.

My experience in the seventy-one cases mentioned shows that the remedy is a convenient one to use for some skin diseases in which small areas only are involved, and for small superficial new growths; that the beta- rather than the gamma-rays are the useful ones, and that some new growths disappear more readily when treated by radium than by the X-rays. It cannot yet be determined whether recurrences are less likely to follow the use of one remedy than the other, but the convenience in the use of radium and its greater promptness of action would indicate that it will be a successful rival of the X-rays in its own limited field.

Francis H. Williams.

The bibliography contains a list of books of interest to those studying the use of the X-rays and radium in medicine.

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LIFE ASSURANCE

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LIFE ASSURANCE, although scarcely two centuries old, bids fair soon to embrace the whole civilised world.

The casualties of life have become matters of scientific prediction; what seemed to be "accidents" are seen to be less and less under the dominion of "chance," which, indeed, is but a word to express our ignorance of the laws in operation.

The likelihood that a confidential servant will betray his trust can be estimated and provided for with the same precision as the probability of the occurrence of a storm, a shipwreck, a murder, or a suicide.

The medical selection of lives was not attempted in the early days of life assurance. The first life assurance society, "The Amicable," was founded in 1706, and existed for years before a medical officer was appointed. The same premium was paid by each applicant, whatever his age or apparent health. He was, however, called upon to state on oath that he believed himself to be a good life.

In process of time it was found desirable to exclude manifestly unhealthy applicants. Hence the proposer was required to appear before the Board. Some directors were shrewd in their judgment as to the value of a life, but it soon became apparent that a medical inspection was required for the selection of "first-class lives." The "Clerical and Medical Life Assurance Society" was the first to grant policies on "invalid lives" in 1824.

Besides the health, the age of the life to be assured needs consideration, and the duration of the term of the assurance.

The premium required being greater in proportion to the age or "expectancy of life," it is customary for the medical adviser, in estimating the necessary addition, to ask himself the question, "Will the applicant before me, now 30 years of age, live as long as a healthy man at 35, 40, 45, or 50?" If he considers that the "expectancy" of the invalid life before him is as good as that of a first-class life at 45, he advises the addition of fifteen years in estimating the annual premium.

Other questions, besides the medical selection of lives, call for the attention of the profession, and though in the domain of the actuary have intimate relations with medical and medico-legal science.

Term Policies are issued for short or long periods, of days, months, or years; a life may be accepted for a "short term" when uninsurable for a long one. Some disabilities that prevent the acceptance of the life may, however, so greatly increase the danger of speedy death as to demand the refusal of the risk, even for a few weeks; this is especially the case if the "habits" are bad. The premium receivable for a short period being very small, the loss involved in the event of a claim occurring is so great that no ordinary addition to the premium would cover the risk. In these cases a large premium, say 3 or 4 per cent, is sometimes suggested instead of the usual addition of years.

Contingent Risks, or assurance payable only in the event of one person, generally young, dying in the lifetime of another, are rendered unduly dangerous to the office if the younger life is a seriously damaged life. A high extra rating may then be insufficient to cover the risk. Thus a "weedy" youth at 25, whose habits are uncertain, may be ineligible against a healthy life at 50, though insurable for life with an addition. The medical examiner thinks only of the case before him; the actuary reminds him that, whilst the loss on a particular case might be comparatively large, the greater number of the "contingent risks" are never heard of again by the doctor or by the Board; they become void by reason of the death of the older life, or are dropped, the assurance having been effected for temporary purposes.

Furthermore, the mortality among recently examined lives (say within five years) is less than the tabular rate; consequently, for all forms of assurance where the period (five years) forms a considerable portion of the risk, the calculated premium is slightly in excess of the true net premium, and the "loading" in contingent cases is usually heavy.

Issue Risks are often affected when the "heir presumptive" wishes to raise money on his expectations, there being no "heir apparent"; also when it is desired to quash a trust in favour of children, a marriage having been childless. In such a case the risk to be considered is not so much of issue by the existing marriage as of the death of the wife and remarriage of the husband; the chief considerations being the health of the wife, and the prospect of the man marrying again late in life and having children. If the wife's health be uncertain, the prospects of a

second fertile marriage by the man may be considerable. Witness the following case:—Policy 6142, 5th May 1881, £5000, single premium £262 : 10s. (£5 : 5s. per cent). A. B., born 1814 (æt. 66); Mrs. A. B., born 1813 (æt. 67), died 1886, æt. 72. A. B. remarried in 1890 (æt. 76) C. D. (æt. 19), and had issue (boy) 1892. A. B. died 1896 (æt. 81). Claim paid 1896—the loss on this issue-policy being slightly more than 90 per cent.

The cause of sterility in the woman often needs consideration. If this be removable, the risk, of course, is greatly enhanced. Sometimes the issue risk to be covered is not only the birth of an heir, but his attaining the age of 21. A variety of issue risks has been proposed in which the probability of a woman, known to be pregnant, giving birth to viable twins has to be considered. In certain families and with certain individuals the probability of twin births is enhanced.

Endowment Assurances payable during life, say on reaching the age of 50, 55, or 60, have tended to modify the work of a medical examiner by increasing markedly the proportion of "first-class lives." A proposer having a shrewd, perhaps well-grounded, suspicion that his life will be a short one, in his natural endeavour to pay as little as may be for his privileges, is likely to select a whole-life "without profits" policy, rather than a short-term endowment which would double the annual premiums.

It is on this account that the medical examiner should scrutinise with especial care the "without profits" whole-life policies, and look with a favourable eye on the short-term endowments.

Members of the medical profession, who feel that Life Assurance is a business of which they have some special knowledge, tend more and more to regard endowment assurances as a safe and remunerative form of investment in which they can obtain 3, 4, or even possibly 5 per cent compound interest on their yearly savings, besides the security of an ordinary life policy in case of premature death. A man æt. 25 may, for annual payments of £28, secure an endowment of £1000 which, on attaining the age of 60, may amount with bonus additions to about £2000. At æt. 35, his practice having increased, he may take out another policy for £2000 at an annual payment of £83, so that on reaching 60 (when perhaps his powers are waning and his professional income diminishing) he receives, say, £4500, and has no further premiums to pay. The claims on this class of assurance are exceedingly small. When any cause, hereditary or personal, leads to the anticipation that the life will not be prolonged much beyond æt. 60, although normally secure up to that time, it is becoming customary to advise "endowment" for such cases; thus, perhaps, the remarkable absence of claims in this class may be somewhat modified.

The relative duties of chief medical officer, medical referee, and medical attendant need definition.

It is undesirable that the *ordinary medical attendant* should act as medical examiner for an office, although occasionally there is no alternative. If he undertakes to report, and accepts the fee, he is bound to

consider the interest of the office first, and that of his patient as of secondary importance; motives of personal friendship must not influence his report.

The **medical examiner** is the adviser retained by the office, and is bound to consider the interest of the office as paramount. He must not allow himself to be swayed by the arguments pressed upon him, often with undue insistence, by the "agent," whose interest it is to carry through business, however insecure. The facts which the agent will supply may be valuable, but are apt to be one-sided and to need discriminating interpretation.

In some offices, where the desire to get business is great, the actuary may also try to put undue pressure on the medical referee, who must then remember that he is responsible to the directors, and is bound to consider first the well-being of the office. Whilst it is the function of the agent, and in a measure also of the actuary, to "carry through" every proposal, it is for the doctor to separate the wheat from the chaff, and to refuse insecure lives.

When an agent finds it difficult to mould the medical examiner, he is apt to try to take the proposer to some medical friend whose opinion he can dominate; hence it is important not to accept the report of an unauthorised examiner without full and satisfactory explanation. A large number of bad lives are thus insured in offices which do not insist upon reports from a medical referee of their own selection.

In his **personal examination of an applicant** each medical man should follow the methods of diagnosis to which he is accustomed.

He should take note of the condition of the heart and great vessels, the lungs, the kidneys, etc. He will probably learn much from the character of the pulse and cardiac rhythm, and still more from the aspect, the morale, and general physical condition.

Whilst taking pains to investigate the case and estimate exactly the probabilities of life, the medical examiner should avoid over-examination. Would-be insurers are frightened away by too elaborate an investigation and too exacting an air. It is not necessary in every case, as some morbidly conscientious tyros seem to think, to use sphygmograph, laryngoscope, ophthalmoscope, and so forth. When the office is represented by a competent and carefully selected medical adviser, the end sought is best obtained without insisting on the registration of pulse, respiration, temperature, and quality of heart and lung sounds in various situations. Such formal inquiries tend to draw away attention from essential points, and vitiate, if they do not destroy, the value of the report. Even if now and then an obscure point be missed, the office gains on the whole by not exacting too minute an investigation and asking too many questions.

An experienced medical man should not take very long in deciding "yes" or "no," and he should not look too critical or "difficile."

If he himself has to labour through an endless series of questions, many of them trivial (for example, colour of hair and eyes) and non-

sensical (for example, "of what temperament is the applicant?"), he has little time or spirit left for forming an independent opinion, or for the exercise of that sagacious and comprehensive judgment which, after all, is the thing sought.

Some offices receive reports from medical men having scanty experience of assurance practice, as is seen by their conclusions, which have but little relation to the observations on which they are based. Thus cardiac imperfections or albuminuria are mentioned, and yet the case is recommended at ordinary rates, or perhaps with an addition of three years: or a high loading is suggested with nothing in the body of the report to justify it, except perhaps hernia or doubtful family history.

Offices whose forms are filled up by all sorts and conditions of medical men may find it of use to try to obtain facts rather than inferences; but where competent men are selected to make the examination, the simpler the form the more valuable the report. The following simple forms have been proved by long experience to be useful ones. They give an opportunity for stating in order the points likely to be of most importance for the consideration of the chief medical officer.

If an application be made to the "medical attendant," Form No. 2 is suitable.

FORM A. NO. 1.

Questions.

Name, residence, occupation, age.

Are you married? Have you visited the tropics, when, and for how long? Are you now in good health? Is your health generally good? What medical or surgical assistance have you required, and when?

Have you any reason to suspect yourself liable to any affection of throat, lungs, heart, or any other organ?

Do you know of any hereditary disease in your family, such as asthma, consumption, insanity, scrofula, cancer, or gout?

Family History

Father, mother, brothers, sisters, age if living; if dead, at what age and from what cause? Is your family a healthy one?

I declare foregoing particulars to be true (to the best of my knowledge and belief). Signature of proposer.

The medical officer is then requested to report the result of his examination and inquiries in the following form:—

Height and weight of applicant (about). State of lungs, as shown by physical examination. Hæmoptysis. State of heart (by physical examination). Pulse. Gout or rheumatism. Digestion and abdominal organs. Genito-urinary system.

As to habits, whether regular, temperate, and healthy; occupation and pursuits, whether or not detrimental to health. If a woman, state of uterine functions.

Is there any other circumstance calling for remark?

From examination, do you think he seems likely to live as long as any other person of his age, and do you recommend his life to be accepted?

If so, whether at ordinary rate?

If not, what addition to the age do you advise?

Signature of medical referee, address, qualification, date.

Form No. 2

Confidential. How long have you known Mr. —— ? Are you in the habit of seeing him frequently? For what diseases have you attended him?

When did you last see him professionally, and for what disease?

Has he, to your knowledge, ever had any serious illness for which he has been attended by any other medical man?

Has it come to your knowledge that any of his near relations have suffered from consumption or any other hereditary disease? State what you may know, or are able to ascertain, of the health and longevity of his parents and other near relations. Do you consider that he is now in good health, that his cerebral, thoracic, and abdominal organs are sound? If not, state in what respect they deviate from health.

Is he temperate in his habits? What are his pursuits, and are they detrimental to health?

Is his physical conformation such as is consistent with a fair average life? Is he likely to live as long as any healthy person of his age? Do you consider that on the whole his life is a first-class one? If not, state the grounds on which you form your opinion, and the addition you think should be made to his age to meet the extra risk.

A space is left for any "special question" which the actuary or chief medical officer should, from other information, deem important, and a space left for signature, qualifications, and date.

The medical examiner should secure a private interview, for in the presence of the agent, or of any friend or relation, people are apt to be less frank and unconstrained. The proposer should be placed as much as possible at ease, and the inquiries should be made with quietness, courtesy, and deliberation. The proposer should realise that he must give honest answers to definite questions, which are neither impertinent nor inquisitorial. Directors are rightly severe in refusing applicants found to be tricky and secretive; when a proposer is detected in making a false statement it is right to decline to accept him. Life assurance should be an honourable transaction for mutual advantage, and an attempt to overreach should not be lightly passed over by either party.

Preparation for Medical Inspection.—Before venturing to appear for medical examination many candidates take a bath, visit the barber, attend to the tongue, the teeth, and sometimes consult their family doctor that "they may be put in order" and be prepared for the ordeal. They also avoid giving any information about family and personal history which might lead to an extra rating, and dexterously omit all incriminating details.

Tropical Rating.—The practice of applying an extra rating for residence in the tropics, whilst giving occasion for criticism on the part of those who disapprove of the imposts, has been found to work fairly on the whole. The risk of death in the early years of tropical life is considerable; it should be also remembered that an extra payment is demanded only during residence in the tropics, and is taken off when the proposer returns to Europe, perhaps with health broken by tropical disease.

The habit of "rating-up" for tropical fever, ague, dysentery, etc. (those who come for assurance after living abroad), is also fully justified by experience, as also are the ratings for "active service in the field."

Ratings for **dangerous avocations** call for consideration; among these the most frequent are occupations connected with the drink trade. It is customary to add a 50 per cent extra to such cases, even if classed as "A1" by the medical examiner; but it is probably wiser to follow the rule of the more cautious offices, and absolutely to decline to accept proposals in such cases.

Extra risks arising from hunting and other active sports, which occasionally lead to a broken neck or concussion of the brain, may be accepted at ordinary rates on the ground that the improved health and longevity secured by an active, open-air life will more than counterbalance the extra risk.

Details regarding the diagnosis and prognosis of well-defined diseases may be dispensed with, but there are various conditions of imperfect health more difficult to assess concerning which something must be now said.

Susceptibility to disease, whether catarrhal or zymotic, exhibited by the proposer or his family needs consideration. Vulnerability means increased risk and therefore extra rating.

Obesity.—Among conditions which may not be classified as "disease," or even "impaired health," undue stoutness, or excessive weight in proportion to height, calls for consideration. If obesity do not directly shorten life, it greatly increases the risks from acute and chronic disease. When an effort is needed to meet some unexpected strain, a large extent of useless, cumbersome tissue, a fatty heart, loaded liver, restricted lung surface, or kidneys prone to disease, become powerful allies of any intercurrent disease in the assault upon life.

As soon as a man's weight increases much above the average weight (see table), and the abdominal girth exceeds the chest girth, an extra rating is called for. Weight alone, without consideration of the build, the size of the bones, the conditions of the muscles, etc., is not a sufficient guide. Flabby muscles, pendulous abdomen, insufficient exercise, and excessive food are conditions incompatible with prolonged health. A man, æt. 40, who, since the age of 20, has steadily increased in weight and bulk, and finds his breathing short on exertion, should not be accepted without an addition of five years, even though in all other respects he may seem well. Experience has shown (see *Report on Invalid Lives*, Equity and Law Assurance Society) that cases rated upon the

ground of "stoutness" have proved a very unfavourable class. Habits of excessive eating and drinking and insufficient exercise tend to shorten life, and the very obese must be declined, or accepted for short terms with high rating.

Leanness.—When the weight is markedly below the average, careful investigation as to the cause is required. If loss of weight be progressive the risk is enhanced, and the necessity for an explanation of the cause essential. It may be an early indication of phthisis, diabetes, cancer, or other progressive disease in the organs of digestion and assimilation.

TABLE OF HEIGHT AND WEIGHT.

Feet	Inches	Stones	Lbs.	Feet	Inches	Stones	Lbs.
5	3	8	13	5	10	12	4
5	5	9	11	6	0	13	5
5	7	10	10	6	2	14	7
5	9	11	10	6	4	15	9

If due to unusual slimness this need not necessarily imply delicacy or vulnerability, for the thin and "wiry" are (proverbially) long lived, or at least have so great an aptitude for recovery from disease as to justify their acceptance without extra rating, if careful inquiry elicit nothing against the life.

Leanness, associated with feeble physique, calls for a considerable "extra." A man, 5 ft. 7 in. in height (see table), whose weight is but 8 st. 10 lbs. instead of the normal 10 st. 10 lbs., is probably a better life than a man of the same age who weighs 12 st. 10 lbs.; or a man, æt. 40, 5 ft. 10 in. in height, weighing 10 st. 4 lbs., instead of the normal 12 st. 4 lbs., is a more favourable life—other things being equal—than if his weight were 14 st. 4 lbs.

Two stone above or below the normal need not in either case necessitate extra rating, but extra caution is demanded. Note should always be taken of such deviation, and if no explanation be forthcoming adequate ground exists for extra rating.

Heredity.—Longevity is hereditary in some families, as is premature death in others (see *Analysis of Peerage Mortality*, Sprague), and this without noticeable strength or feebleness of physique.

When a tendency exists in the line of both parents to any special disease the heredity is intensified, notably in phthisis, cancer, and insanity.

As with phthisis, hereditary gout is manifested earlier than the acquired form. If a tendency to gout or asthma exist on both sides a considerable extra rating is called for; where cancer is doubly inherited it is safer to decline, or to require all premiums to be paid by the age of fifty. Where one parent only has suffered from gout, rheumatism, heart disease, diabetes, or cancer, this may be overlooked if the case be otherwise unexceptionable.

An investigation into the life and health of grandparents, aunts, cousins, is usually supererogatory, but the medical referee may be often aided by such an inquiry; he should never omit to report on the brothers and sisters of the proposer.

Phthisis.—As one death in nine is attributed by the Registrar-General to tuberculosis, its early detection is of primary import; and as the mortality from phthisis among assured lives is but eight per cent, it is evident that medical selection has proved of value. Half the mortality from phthisis among the assured occurs before the age of 40, and three-quarters before 50.

The occurrence of **hæmoptysis** needs careful consideration; if following strain, and there be no evidence of inheritance, of heart or lung defect, of wasting or constitutional disorder; and if the applicant have passed the age of 30, the life may be accepted with a slight addition. Where hereditary tendency exists, and the chest is long and narrow, the weight light, and the pulse quick, the life should be refused. Indeed, the coexistence of hæmoptysis with a history of hereditary phthisis would call for refusal.

In insurance practice, where the opportunities for complete examination of a case are limited, it may not be easy to make a prognosis with adequate confidence to justify the acceptance of a life with serious organic disease; but *every life has its value*, and, with advancing pathological knowledge, accurate clinical methods, and acquaintance with the natural history of disease, a prognosis may be made with sufficient precision to justify the acceptance of the risk. This is certainly the case with the varieties of *valvular disease of the heart*, and in some cases of chronic *fibroid change in the lung* the life may be assessed with equal confidence and accepted with extra rating for short periods, or under the "endowment" or "limited payment" system. In cases of this class, however, the chief medical officer would probably require to see the case himself, and would not recommend it to the acceptance of the Board on any second-hand information.

Emphysema, when associated with chronic or recurrent bronchitis, especially if any signs of commencing cardiac dilatation exist, must be refused. If a somewhat inelastic chest wall, a prominence of thoracic venules, and tendency to dyspnœa on exertion, alone mark the emphysematous tendency, or if only occasional asthmatic attacks are recorded, an extra rating will suffice. Liability to bronchial attacks, whether of gouty, syphilitic, or phthisical origin, renders the life precarious even for very short terms.

Pleurisy.—Where traces of pleurisy exist, if the proposer be young, and if family and personal history, aspect, pulse, etc., should point to a possible tuberculous origin or complication, the case should be declined. If the evidence indicate no more than the local contraction consequent upon old pleurisy of non-constitutional origin, a small extra rating will suffice.

Heart Disease.—The diagnosis and prognosis of cardiac disorders are

fully discussed elsewhere; I can only say here that cases in which indications of muscular failure exist are uninsurable. Where compensatory hypertrophy conceals all evidence of circulatory defect the case may be considered, and acceptance advised on condition that all premiums be paid before degenerative changes are likely to occur. Aortic disease is more perilous than mitral. Cases of mitral stenosis and aortic regurgitation can but seldom be accepted. Less, however, depends on the situation and character of the murmur than on the history and constitutional state.

Irregular action, with feebleness of impulse and confused rhythm, is of evil portent.

Intermission of the pulse and apex beat may not prove the existence of serious defects, but calls for close investigation, and often leads to the discovery of gouty, dyspeptic, or nervous disorder.

The rapid, nervous, palpitating "insurance heart," so constantly observed among candidates for life assurance, requires skill and experience for its estimation. The beat is so rapid, tumultuous, bouncing, and diffused that it suggests the idea of serious disease, and may indeed mask organic defect. Its variability and manifest association with general nervous perturbation will generally enable the physician to assess its import at the first interview; if not, a second should be arranged. Some proposers faint when thus examined, and may justly be regarded as too unstable to be accepted as first-class lives. These are persons who are morbidly sensitive to a refusal or an extra rating, and it is important by firmness and kindness of manner to give them confidence and self-reliance. A medical referee cannot be too careful to avoid causing distress or anxiety in an applicant, even if he be obliged to decline the proposal.

Gout.—The bearing of gout on life assurance is important. Experience proves that a high extra rating is necessary. Gout was regarded in the early days of life assurance as conducive to longevity. The free imbibition of port was followed by occasional explosions, recurring for a quarter or perhaps half a century, and leading to no marked deterioration. In recent years the wide extent of gout, as a constitutional affection leading to heart, kidney, liver, and more general tissue-change, has been recognised even when no joint affection has occurred. Gout, as we know it now, calls for rejection in a large number of instances; and an average addition of 20 to 25 per cent in cases recommended for acceptance.

It must be remembered, too, that while phthisis is a "diminishing risk," gout is an "increasing" one. The mortality from phthisis occurs mainly in early manhood, that from gout in the years when life assurances are most usual, namely, between 50 and 60.

The close relation often existing between gout and **intemperance** in eating and drinking must not be forgotten; the extra rating applied for "gout" might in some cases be more accurately entered under the heading "habits."

No part of insurance medical practice calls for so much discrimination

as this. Intemperance, often markedly hereditary, may show itself in occasional craving for drink or other forms of nerve excitement, and lead to early tissue-degeneration ; the man who indulges freely and continually, because he is never drunk, being in the greater danger. Tact to discern habits of life, and skill to interpret indications (which have been perhaps carefully masked), are essential here.

Among the indications are the hurried manner, loud voice, fœtid breath, bloodshot sallow eye, flushed face, red nose, cold, damp, unsteady hand, tremulous tongue (often clean, especially in women), engorged fauces, carelessness of dress, etc. Where such signs exist, no laboured proof in "friends' reports," or in the statement of the applicant, must be allowed to shake the conclusion of the medical examiner. If he be thus beguiled into accepting a life he was disposed, on personal examination, to reject for "habits," he is nearly sure to hear of the case "as a claim" in a time distressingly short for his reputation and for the office. The evidence as to the "temperance, soberness, and chastity" of a suspected applicant must not always be estimated by the weight or volume of the letters supplied in "friends' reports" !

It is not customary to regard **hernia**, if a suitable truss is worn, as a reason for extra rating. Neither need **piles** nor **varicose veins** be so regarded, except in so far as they give evidence of hepatic engorgement.

A history of **fistula**, if connected with piles which have been cured, does not call for surcharge ; but when there is any evidence of phthisis or constitutional weakness the proposal should be declined.

History of **gonorrhœa** justifies an extra rating ; even when not followed by stricture, etc., it often brings in its train prostatic and vesical troubles which shorten life.

Syphilis.—During the existence of this disease in any primary form the proposal must be postponed.

If any secondary symptoms exist in a quiescent state an addition of five or seven years is required. When these symptoms have been in abeyance for two or three years only the case is not eligible at ordinary rates : it should be rejected if any lesion of brain, spinal cord, arteries, liver, lung, or kidney have occurred.

Albuminuria, whether present or not at the time of examination, if connected with kidney disease, with gouty, rheumatic, or cardiac disorder, or excess in eating or drinking, must be declined.

If the albumin be reported after scarlet fever or exposure, and has been absent for some years, the health being perfect, acceptance may be recommended. Where it has been known to exist for many years without detriment (such cases have fallen under my observation) the case may be accepted, as a case of mitral disease or emphysema might be accepted, with a high rating or for a short term. When a trace only is to be detected, after food, and recurring at intervals, after several examinations at sufficient intervals, and with full knowledge of the case, acceptance, with five, seven, or ten years added, may be advised.

Glycosuria, while it exists, should forbid the acceptance of the proposal. It is often, however, a temporary condition, and may leave no ill effects; unless manifestly due to some transient state, it should be regarded as a ground for refusal, and in any case for addition. In every form of diabetes the risks are too great to justify acceptance. It must not be forgotten that some urines not containing sugar may nevertheless cause a turbidity with Fehling's solution.

In cases of ataxia, and other forms of paralysis of a central kind, refusal is called for. In cases of old infantile paralysis, and in facial paralysis, a moderate extra should suffice (three to five years).

Pregnancy.—Recently married ladies often insure for very large sums, and the risk during the first year of married life is great.

The mortality in first pregnancies is high, and it is wise to defer a proposed insurance until after confinement. It is usual to charge a small—10s. per cent—addition to the first premium for a multipara, 20s. for a primipara. If the age is above 30, and the risk thus enhanced, an addition of 30s. is often justly made.

Claims.—Certificates as to the cause of death should always be considered carefully by the medical officer, and it would be advantageous if a medical report on each claim could be forwarded to the referee upon whose report the life had been accepted. Information to the chief medical officer would become the common property of the medical referees, whose experience would thereby be increased, just as an autopsy is invaluable to the physician who had charge of the case during life.

The wording of the death certificate should be clear and definite. Thus syncope may refer only to the mode of death and have no bearing on the nature of disease. "Childbirth" may mean pulmonary tuberculosis, and should be limited to fatal incidents immediately connected with confinement. "Gastritis" may be a term used to conceal death from intemperance or irritant poisoning. "Dropsy," without evidence of dependence on heart, kidney, liver, should not be allowed to pass without investigation.

If the disease certified as the cause of death existed prior to the completion of the assurance, a question arises as to the *bona fides* of the transaction. If the statements made can be proved false, the claim could not be maintained.

As a matter of fact, offices are most unwilling to refuse any claim; but they have and ought to exercise the power to refuse claims manifestly unjust.

E. Symes-Thompson.

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E. S. T.

THE GENERAL PATHOLOGY OF NUTRITION

By F. W. MOTT, M.D., F.R.S., F.R.C.P.

THE life of the individual is dependent upon the life of the cells or derivatives of the cells, which together make up the organs and tissues of the body. Every cell consists of a mass of protoplasm containing a nucleus, and possesses the property of taking up from the fluid medium by which it is surrounded the substances which are necessary for its vital activity, and of casting out the waste products. It was John Hunter who said: "Every individual particle of the animal matter is possessed of life, and the least imaginable part which we can separate is as much alive as the whole."

Owing to differentiation of structure and specialisation of function, certain master tissues (*e.g.* glandular, nervous, and muscular) possess, in addition to their general functions of repair and waste, a special function peculiar to each tissue involving storage of material. The mammary gland before lactation occurs is in a quiescent state; its cells are living and awaiting the natural physiological stimulus which will arouse their special function of elaboration and secretion of milk; but, prior to this, the cells are still the seat of perpetual inter-molecular rearrangements of matter termed metabolism, constructive and destructive—activities common to all living protoplasm. The most important chemical substances in living matter are the complex nitrogenous compounds termed proteids; they form an integral part of protoplasm, are never found in anything else but protoplasm or that which is formed by the agency of protoplasm; consequently proteid metabolism is an essential characteristic of vital activity.

Physiologically, the cells of the body are dependent upon one another and upon the circulating blood which, as it streams slowly through the capillaries, brings into harmonious relation the effects of each and all of their vital activities. This functional harmony between the different tissues is brought about by the blood, and serves to maintain a constant in the chemical composition and temperature of that fluid; the maintenance of this constant is essential to the well-being of all the cells of the body. There is thus an interdependence of all the tissues; if one suffers, all suffer.

The dictum of Virchow, *Omnis cellula e cellulâ*, is a fundamental principle underlying all physiological and pathological problems. The

fertilised ovum may be looked upon as the fusion of the essential portion of the male sperm-cell with the female germ-cell, and with this process there is a fusion of the properties and attributes of the germinal plasm of the parents. This cell possesses, then, specific properties which distinguish it from every other cell in existence; likewise all the cells which are derived from it by segmentation possess specific vital properties which make them differ from the cells which constitute the tissues and organs of another animal. We may not be able to show by chemical analyses and microscopical examination any differences in the tissues of two individuals; they may seem identical; the distinction, however, appears in the differences of adaptation in the cells of the organism to their environment, individually and collectively. The instability and mobility of the material substance of the cell constitute its life: no portion of the living body is stable, but new formation and regeneration are continually taking place during life, even after completion of the growing period. Many examples of these processes could be cited, viz. the epithelium lining the alimentary and respiratory tracts which is continually being destroyed and replaced; likewise the epithelium covering the surface of the body, and the never-ceasing disintegration and new formation of the blood-corpuscles. The mechanism by which cells are enabled to take up nutrient material from the surrounding lymph and to cast out their waste products is unknown to us. It is a specific property of the protoplasm of the cell, controlled in the higher differentiated tissues by nervous impressions which not only (as may be proved in the submaxillary gland) directly control the functional activity of the epithelial cell-elements, but also the amount of blood flowing through the gland. In health there is a constant *adaptation of repair to waste*; and, although the organic form of the cell or fibre is generally preserved, the contents are continually undergoing molecular and chemical changes (metabolism), with conversion of potential into kinetic energy, consumption of oxygen and organic substances, and the liberation of carbonic acid, water, and other waste products. The energy is replaced and the tissue-waste repaired by the circulating blood. This, however, necessitates a constant in the quantity, quality, and temperature of the blood, which can only be effected by the assimilation of oxygen, food, and water in such proportion as to make up that which is lost to the body by dissimilation in the tissues, and elimination by the lungs, skin, bowel, and kidneys. "A man can live a few minutes without oxygen, a few days without water, and a few weeks without food" (Waller).

The *balance of nutrition* may be maintained when the export is repaired by a corresponding import; and physiologists have shown that the minimum daily income required by a healthy man performing his average daily work, and maintaining his usual body weight, is 5 per cent of that body weight—1 per cent being solid food, 1 per cent oxygen, and 3 per cent water. These amounts may be modified by various circumstances, such as climate, work, age, convalescence from illness, lactation, and the like. An infant or growing child requires food not only for repair

but also for growth. A mother during lactation, over and above the normal amount of nourishment, requires a suitable excess to provide the milk necessary for the suckling infant.

If digestion and assimilation are normal the blood will be maintained at a constant in its chemical composition; should there be, however, an insufficiency of the intake, inanition will follow. Inasmuch as the intake of food is *always intermittent*, and, owing to exigencies in obtaining it, is at times very much so, certain tissues and organs of the body possess *storage functions* which provide reserve material upon which the blood can draw as required. The storage of fat in the connective-tissue and liver cells of the body represents so much potential energy. The glycogen in the liver is a store of carbohydrate which is continually being utilised in maintaining an average constant of sugar in the blood. The sugar is used up continually by the muscles in the production of energy, but if more than a certain quantity exist in the blood, it would be injurious; consequently the liver intercepts the intermittent supply of carbohydrate material in the form of glucose absorbed by the portal blood, converts it into glycogen, and stores it in its cells to be used as required (Bernard). Probably all the cells of the body possess the power of oxygen storage; we have definite proof of its existence in the muscles. The muscles of the frog can contract and produce heat and work in an atmosphere of N with liberation of CO_2 and other waste products; and the muscles of warm-blooded animals will display similar functional activity (when stimulated) for some time after the circulation has ceased. During sleep and rest the tissues are storing up materials for their functional activity; this has been most clearly shown by the histological appearances of the cells of secreting glands during rest and during activity. Another very important factor complementary to destructive metabolism, in connexion with the maintenance of the normal composition of the blood, is what is termed the *internal secretion of glands.*

Blood—the Nutrient Fluid and Medium of Exchange.—The quantity of blood in man is about $\frac{1}{20}$th of the body-weight, and its mode of distribution is varied in accordance with the functional needs of the tissues. Certain organs and tissues, requiring large quantities of blood to perform their functions, are highly vascular in proportion; the supply to a part is regulated automatically by the vasomotor nervous system, and the physiological stimulus which excites the activity of an organ may also determine an increase of blood to the part. Thus, experimentally, an increase of urea in the blood causes an expansion of the kidney due to vaso-dilation, which signifies an increased flow of blood associated with the secretory activity of the organ.

There is an essential similarity between the composition of protoplasm and that of the normal human body—between the normal human body and the circulating blood which provides it with nutrition: for, during gestation *in utero*, a new body is entirely built up from the maternal blood; and there is also an essential similarity between milk, the natural food of the suckling animal, and the composition of the body—with one

important exception to be mentioned hereafter. The cells of the body assimilate from the blood organic proximate principles representing so much potential energy, which they convert into kinetic energy in the form of mental and bodily work.

Cell-activity, then, depends upon chemical action, and the products of cell-activity are carbonic acid, water, and nitrogenous waste products, of which urea is by far the most important.

To restore to the blood that which it has given up to the tissues requires daily ingestion of a certain amount of food in the form of organic proximate principles: proteids, carbohydrates, fats, water, salts, and oxygen.

The proximate principles which enter into the composition of the human body are composed of fifteen elements, united in various combinations to form complex energy-producing organic substances and simpler inorganic substances—the latter incapable of producing energy, but still essential for nutrition, water making up at least two-thirds of the body-weight. The elements contained in the body, and therefore in the blood, are C.H.O.N.S.P.Fe.Na.K.Mg.Ca.Cl.I.F.Si. Although many of these exist in very small quantities, yet in all probability they are essential to the blood for the proper nutrition of the cells of the body. Even fluorine, which exists only in minutest traces, is essential to the formation of the teeth and bones.

"The law of the minimum" holds as good for the nutrition of the human body as it does for agriculture; that is to say, the food must contain not less than certain quantities of the above elements, and in such forms as can be assimilated. Iron is the element of great importance in connexion with the function of oxygenation of the tissues, by means of the iron-containing hæmoglobin. The iron in the body of an average-sized man is 3 to 5 grammes, the greater part of which is contained in the blood in the form of hæmoglobin; the rest is combined with nucleo-albumins of the tissues. Bunge points out that the ash of a bitch's milk corresponded with the ash of the body of the puppy in every respect save one—there was six times less iron. The explanation of this doubtless lies in the fact that the young animal acquires its store of iron during its development *in utero.* The proportional amount of iron to the weight of the body is highest at birth, and gradually diminishes with the development of the animal during lactation. These facts may explain the wonderful effect of small doses of iron and cod-liver oil on the nutrition of ill-nourished, rickety infants, and the advisability of not deferring weaning or not adhering too long to a purely milk diet, but of using food which supplies more iron.

We obtain in our food enough of all the inorganic salts save one—sodium chloride; but our diet is by no means deficient even in this. No animal can live if its food be deprived of salts. It has been suggested that as the blood loses a large amount of its inorganic salts, and these are not replenished by the food, there are no bases to unite with the SO_3 formed by the oxidation of the sulphur of the disintegrated

proteids. It is probable that the salts favour osmotic changes by their power of diffusion; and certain salts, especially sodium chloride, play an important part in nutritive exchange by holding in solution in the blood and muscle-plasma certain proteids of the globulin class. The important part played by lime salts in the formation of bone and by potash salts in the tissues is well known. (*Vide* articles "Rickets" and "Scurvy.")

Proteids are essential to restore to the blood those proteid substances which have been used by the tissues for repairing waste. Muscular energy can be obtained from proteid, but normally it is obtained from carbohydrates and fat, a more economical method. It has been found, however, that proteids alone can repair tissue-waste, and that if proteids are not contained in the food in proper proportion the tissues feed on themselves. In inanition or starvation, on the other hand, a selective process seems to take place, and the tissues which are of the least consequence suffer the most. Fat rapidly disappears, muscle wastes; so also do many of the glands, the spleen, and liver, and even the blood itself; but the circulating medium nourishes the nervous system and heart, so that the master organs essential to the life of the individual may be supported at the expense of the less important tissues. This vicarious nutrition may be considered as a defensive power of the organism to resist dissolution of the nervous system and heart.

Sir Thomas Barlow (in the Bradshaw Lecture, 1894) has shown that condensed milk or even sterilised milk is not an efficient substitute for the natural food of the suckling infant, and that infantile scurvy may be occasioned by their sole use. It is noteworthy that although animals can live on milk alone, yet if a mixture be made of all the supposed constituents of milk which, according to the present teaching of physiology, are necessary for the maintenance of the organism, the animals fed on it rapidly die. Does milk then, besides carbohydrates, fat, proteids, salts, and water, contain other substances indispensable to the maintenance of life?

Of like importance in nutrition are certain phosphorus-containing substances in the body, viz. a phosphorised fat termed *lecithin*, indispensable for the constructive metabolism of the central nervous system and red blood-corpuscles; and *nuclein*, which consists of an organic phosphorus-containing acid, termed nucleic acid, in combination with proteid. The amount of P varies in different forms of nuclein, as the sulphur varies in amount in different forms of proteid. Nucleic acid contains C. H. O. N. P but no S. The nucleus of a cell serves two functions—the nutritive and the formative; it exercises a controlling influence on the nutrition of the cell, and it is in the nucleus that the first evidences of cell-proliferation are manifested. The essential portion of the male sperm-cell, namely, the head of the spermatozoon, chemically consists entirely of nucleic acid.

The composition of cells is mainly *spongioplasm* and *hyaloplasm*; the former is the meshwork in which the latter more fluid protoplasm is

contained. The spongioplasm stains readily, and is therefore called chromatin, a body which contains both P and Fe. Experiments seem to show that the daily output of uric acid is derived from destructive metabolism of nucleo-albumin. If this represent the total N derived from the waste of nucleo-albumin, it shows how very small is the destruction of the fixed framework of the cell-elements, and how carefully these highly complex organic bodies are preserved from waste. The fluid which surrounds and bathes every cell of the body is a transudation from the blood; and it is the property of every anatomical element to take from the fluid the materials which it requires, to incorporate them for a time, to utilise them in various ways according to its special function, and to give back to the fluid various waste products or bye-products, the outcome of its functional activity. There is thus going on in the cells a continual and associated process of *recomposition and decomposition—of constructive and destructive metabolism*—a nutritive exchange essential to all forms of physiological function, whether it be of body or mind.

The deficient supply of blood or deficient quality of the blood is, then, one of the causes of nutritive derangement, and of cell-degradation and death. Another cause may be, *the failure on the part of the organism to eliminate the waste products which accumulate in the blood*, causing injury to the cell-elements, as in uræmia.

Certain Disorders of Metabolism.—A human body in health may be likened to a chemical factory managed upon the most perfect and economical principles. No energy is wasted, all the bye-products are utilised by perfect oxidation processes, the furnaces are kept steadily burning by an adequate supply of oxygen, and the waste products are removed and not allowed to corrode the machinery. The co-ordinating mechanism by which the cells of the living body carry on so many and varied chemical processes, involving oxidation, hydration, dehydration, and complex synthetic processes, is an automatic associative memory of experiences which in the infinity of time have served for the preservation of the individual and the species. Thus it is that the initiation of the chemical processes of digestion should, as Pawlow's beautiful experiments have demonstrated, always start with a desire for food, which causes an increased secretion of gastric juice ("appetite juice"). The desire may be excited by hunger or by the stimulation of the special senses of taste and smell. The co-ordination of the activities of associated organs may be effected, not only by the nervous system, but also by the intermediation of chemical substances produced in one organ and carried to the other by means of the blood-stream. Such bodies have been termed by Professor Starling "hormones" (from ὁρμαω, I excite *or* arouse). The best example of such a chemical reflex is furnished by the pancreas. Whenever acid is introduced into the duodenum, there is a responsive flow of pancreatic juice. Drs. Bayliss and Starling have shown that this flow occurs when all nervous connexions between the duodenum and pancreas have been destroyed. The carrier of the message in this case from duodenum to pancreas is a body they call secretin, which is produced in the intestinal

epithelium under the influence of the acid and carried thence by the blood to the pancreas, where it acts as a specific excitant of the secretory cells. The more automatic and the less conscious the individual is of these chemical processes the more perfectly are they being carried on; in fact, the healthy individual should not be aware of the organic functions of the body except at periodic intervals when the appetite and desires which are the normal stimuli to the activity of certain organs, such as the digestive and reproductive glands, intrude on his consciousness. Other organs of the body, *e.g.* the kidneys and liver, are continuously and unconsciously performing their functions. Any breakdown of the chemical activities of an organ or tissue of the body makes itself evident in various ways; but whatever the means by which we are made conscious of the failure of function, it must be looked upon as protective to the organism, *e.g.* the malaise and headache of various toxæmic conditions, incidental to liver and renal inadequacy; the heart-burn and eructations of gastric catarrh and imperfect digestion; the colic and diarrhœa caused by chemical irritants in the intestines, generally the result of improper food. All these symptoms should not be regarded as baneful because they disturb our sense of well-being, but as protective calls of nature for assistance, or as a warning demanding the renunciation of bad habits. The cells of the social organism not only act in harmony in nutrition and repair of waste but in defence against disease. The defences of the organism are directed chiefly against bacteria, bacterial toxins, and poisons introduced from without or formed during digestion or during metabolism. The important subject of immunity, or the bactericidal properties of the blood and lymph, is dealt with elsewhere, and will therefore not be considered in this article. The chemical defences of the organism may be considered under the following headings: (1) Oxidation processes occurring in the tissues and their associated decompositions; (2) The processes of hydration and dehydration; (3) Synthetic processes.

OXIDATION PROCESSES.—*Tissue Respiration.*—In the passage of the blood through the pulmonary capillaries oxygen is taken up by and becomes loosely combined with the hæmoglobin; carbon dioxide being excreted by a process of decomposition of the sodium bicarbonate into sodium carbonate, carbonic acid, and water. This is a process of oxygenation of the blood, and must be distinguished from the process of oxidation which takes place in the tissues. As the blood slowly streams along the delicate-walled capillaries of the tissues, the feeble link which holds the oxygen in combination with the hæmoglobin is unloosened; this is probably brought about by the carbon dioxide, which, owing to the increased tension, has always a tendency to pass from the tissues to the blood, but having reached the blood it immediately combines with the sodium carbonate, forming a bicarbonate; at the same time an unlinking of the oxygen molecule from the hæmoglobin is effected. Now there is never any free oxygen in the lymph bathing and permeating the protoplasm of the living cells, for as fast as it diffuses through the capillaries it is taken up and immediately consumed in the processes of oxidation by the cells

or stored up for future use. All proteids contain traces of iron, especially the nucleo-proteids, and it is therefore conceivable that the oxygen unites with this iron to form a substance analogous to a ferric salt, and that in the processes of reduction incidental to active oxidation there is a change analogous to the reduction of a ferric to a ferrous salt. Admitting this hypothesis as possible, it does not explain how the oxygen which is continually being picked up by the ferrous and converted into ferric substance can, by a process of reduction from ferric to ferrous substance, liberate oxygen capable of burning up fat and sugar at the temperature of the human body. It can be shown experimentally that the living tissues of the body possess oxidising powers; thus a parenchymatous organ reduced to a fine pulp will, if brought into contact with formic aldehyde, oxidise the latter into acetic acid, though it has no effect on sugar; but it must be remembered that sugar cannot be utilised in the absence of the glycolytic ferment of the pancreas, and therefore accumulates in the blood, causing pancreatic diabetes. Having discussed the possible mode in which the cells of the organism take up oxygen and give off carbon dioxide in the metabolic processes incidental to their functional activity in the production of heat, and their specific energies, nervous, muscular, and glandular, we will briefly discuss the source of the energy, the mode by which the waste is repaired, and the excreta eliminated.

Physiology teaches that to maintain nutritional equilibrium a definite quantity of proteid is essential, and that life can even be maintained on a solely proteid diet. It was at one time considered that the minimum proteid intake should represent not less than 15 grammes of nitrogen; but Chittenden by his experiments on "Physiological Economy in Nutrition" has conclusively demonstrated that a man can keep in perfect health and perform daily vigorous bodily exercise on a proteid intake representing 9 grammes of nitrogen, provided he chews his food thoroughly and that his diet contains a quantity of carbohydrates and fats sufficient to supply the active energy produced by cell-metabolism. Certain slow, insidious, degenerative processes, diseases, and terminal toxæmias engendered and caused by the imperfect oxidation of the products of proteid metabolism and their elimination, are the result of continued excess of proteids, especially nucleo-proteids, in the diet of persons who, from inherent or acquired metabolic defects, organic disease of the depurative organs, *e.g.* liver and kidneys, are unable to oxidise and eliminate completely the waste products of the *luxus* of proteid consumption. The signs of disordered metabolism are loss of body-weight, inanition, increase of body-weight, obesity, loss of sense of well-being, modification of the temperature of the body, alteration of the respiratory quotient $\frac{CO_2}{O}$; changes in the quantity of urine and of its normal constituents and the presence of abnormal constituents. Most of these conditions of disordered metabolism are discussed fully in special articles to which the reader is referred, so that it is only necessary to allude briefly to the facts concerning the digestion and absorption of food-stuffs.

Food-stuffs, generally taken into the body in a solid form, are, by the action of the hydrolytic ferments of the digestive juices, rendered soluble and diffusible, or so acted upon that they can be assimilated by the living epithelial cells and leucocytes of the mucous membrane of the alimentary canal. The fats are saponified or emulsified, and the carbohydrates are converted into glucose. The sugar in health is not allowed to exceed a percentage of 0·02 to 0·05 in the blood; for any excess is by a process of dehydration in the liver converted into glycogen and stored up in the liver cells. The large complex proteid molecule is by a process of hydration converted first into proteoses or albumoses, then into still smaller molecules of peptone, next into groups or chains of amino-acids, termed polypeptides by Fischer, and finally into the amino-acids themselves, which fall into three main groups:—(i.) Mono-amino-acids, such as glycin and leucin; (ii.) Di-amino-acids or hexone bases, such as argenin; (iii.) those containing an aromatic radical, such as tyrosin. These amino-acids yield but little energy, and probably the bulk of the *luxus* of proteid consumption is converted into these bodies. Although it is believed that the absorptive epithelium has the power of resynthesising proteids from their simple cleavage products, it can, however, hardly be doubted that a large proportion of the amino-acids never take part in this synthesis, but are rapidly removed from the body as urea. It is generally believed that leucin and tyrosin are converted into urea in the liver on the grounds that in acute yellow atrophy and in some cases of phosphorus poisoning urea is greatly diminished, while at the same time leucin and tyrosin appear in the urine; it is probable, however, that some of the leucin and tyrosin in these morbid conditions is derived from the destruction of the liver substance. Ammonia formation is an intermediate stage in the formation of urea. There is experimental evidence (by Eck's fistula) to show that the nitrogenous products of proteid digestion are converted by the epithelium of the alimentary canal and the liver cells into ammonia, and that this ammonia unites with the carbon dioxide, simultaneously formed by the cells in the processes of oxidation, to form ammonium carbonate, $O=C\langle{}^{O\,.\,NH_4}_{O\,.\,NH_4}$, which is in turn converted into ammonium carbamate, $O=C\langle{}^{NH_2}_{O\,.\,NH_4}$, and eventually into urea, $O=C\langle{}^{NH_2}_{NH_2}$. But since ammonia is formed not only by the liver cells but by all the cells of the body in which active metabolism is proceeding, it follows that urea is manufactured by the tissues of the body as a whole and not exclusively in the liver, although the final synthesis into urea occurs mainly in that organ. The formation of urea from ammonia is of particular interest in connexion with the following subject.

Acidosis or Diminished Alkalescence of the Blood in Relation to Disordered Metabolism.—The ammonium salts of the blood may be increased considerably if the oxidation processes of the liver and tissues are interfered with, and inasmuch as these salts are much more toxic than urea, symptoms of poisoning may arise. Under certain conditions

the ammonium salts may be greatly increased at the expense of the urea; this indicates that the blood contains more than the normal amount of ammonia, and that tissue-metabolism is in a disordered condition. In diabetes, especially when there is impending coma and the breath smells of acetone, β-oxybutyric acid ($CH_3 . CHOH . CH_2 . COOH$) and diacetic acid ($CH_3COCH_2COOH$) are formed in excess and accumulate in the blood, and the condition termed *Acidosis* results. This acid condition of the blood is believed to give rise to coma in the following way. The β-oxybutyric acid unites with the sodium salts, of which there is only a limited quantity, in the blood, and thus interferes with the process of tissue (or internal) respiration described above (p. 541). In addition to the sodium salts, the ammonia is used to neutralise the acid, as is shown by a great increase of the ammonium salts in the urine, and the native alkali of the blood is thus to some extent spared. In health only about 5 per cent of the nitrogen output in the urine is in the form of ammonia, but in diabetes it may be as much as 20 per cent of the total nitrogen excreted, amounting in some exceptional instances to as much as 8 to 10 grammes per diem. The quantity of ammonia in the urine serves as a rough index to the degree of acid intoxication. A much more accurate estimation can be obtained by a determination of all the bases, sodium, potassium, magnesium, calcium, ammonium, in the urine, and comparing their total alkali value with the total acid value of all the known acids, hydrochloric acid, phosphoric acid, uric acid. As compared with normal urine, that of a patient suffering from severe diabetes with threatened coma will show a great excess of bases unaccounted for by the normal acids. Since this large excess of basic material is not present as free alkali in the urine, it must be combined with some acid not present in normal urine. The acid is mainly β-oxybutyric acid ($CH_3 . CHOH . CH_2 . COOH$), or an amino-derivative of this acid (Grube).

In some instances, especially when diabetic coma is impending, diacetic acid (CH_3COCH_2COOH) occurs in the urine, and some authorities ascribe to it a principal part in the causation of coma. The acid intoxication therefore leads to withdrawal of alkaline salts from the organism, and thus accounts for the symptoms which arise. As long as the cells of the body are able to supply sufficient ammonia for the neutralisation of the organic acids found in the body, the alkalinity of the blood is not seriously disturbed. As soon, however, as the source of this alkali fails to neutralise the acid completely, the sodium and potassium salts of the blood are sacrificed, and the alkalinity of the blood is considerably and permanently diminished. The resulting condition is incompatible with the normal respiratory changes of the tissues carried on by the alkaline carbonates. Some writers are disposed to contest the view that diabetic coma depends upon an acid intoxication, and refer the conditions to toxins. Herter remarks: "The evidence on which I lay most stress consists, first, in the regular development of coma or stupor whenever the excretion of acid is very large; secondly, the absence of typical diabetic coma when there is little or no excretion of acid; and thirdly, the

remarkable improvement in the psychical state that follows the restoration of the alkalescence of the blood by the direct infusion of an abundance of alkali."

A patient on a restricted diet will pass oxybutyric acid, but he will pass more if carbohydrates are added; it is possible, therefore, that the oxybutyric acid may be derived in the case of the restricted diet from the carbohydrate radical of the proteid molecule. But the exact mode in which oxybutyric acid is formed is not known, although it is probably a result of imperfect proteid metabolism.

The best method of estimating the amount of oxybutyric acid in the urine is as follows: Concentrate the urine and distil with strong sulphuric acid; the oxybutyric acid is decomposed into crotonic acid and water ($CH_3CHOH \,.\, CH_2COOH = CH_3CHCH \,.\, COOH + H_2O$), and the crotonic acid can easily be recovered from the distillate.

Cleavage of the proteid molecule not only provides carbon, which can be utilised for the production of energy or stored in the form of fat or glycogen, but ammonia, which serves a useful purpose in diabetes by neutralising the oxyacid products of deranged proteid-metabolism. The experimental observation that much smaller doses of mineral acids are required to kill herbivorous than carnivorous animals has been explained on the ground that the former produce much less ammonia. The production of ammonia then may, in certain abnormal circumstances, constitute a chemical defence and be a means of maintaining the alkalescence of the blood so essential for cell respiration and vital activity. Other normal processes have a similar action; one, which is continuously in action, is the secretion of acid sodium phosphate in the urine; another, which is intermittent, is the secretion of the acid gastric juice. The phosphoric acid of the blood, which is in the form of phosphates of potassium, sodium, and calcium, comes partly from the phosphates of the food and partly from metabolic oxidation of the phosphorus-holding cells of the body. The phosphoric acid thus formed unites with sodium bases to form the di-sodium phosphate. The blood cannot contain either free phosphoric acid or the mono-sodium phosphate, but the urine contains this salt and owes its acidity to it, and it may be assumed that the renal epithelium effects a rearrangement of ions by which there result mono-sodium phosphate and sodium carbonate.

$$CO\begin{cases} OH \\ OH \end{cases} + PO\begin{cases} ONa \\ ONa \\ OH \end{cases} = PO\begin{cases} ONa \\ OH \\ OH \end{cases} + CO\begin{cases} ONa \\ OH \end{cases}$$

The acid salt $Na \,.\, H_2PO_4$ passes into the urine and the alkaline bicarbonate is returned to the blood. The hydrochloric acid formed in the stomach leads to an increased alkalescence of the blood; the chemical change being represented by the following equation: $NaCl + H_2O = HCl + NaOH$. The sodium hydroxide is immediately converted by the carbon dioxide of the blood into carbonate of sodium, and some of the

sodium carbonate thus returned to the blood is utilised in providing the alkali of the pancreatic juice. The secretion of gastric juice, then, is not only necessary for digestive purposes, but is important in other ways in the chemistry of nutrition. In fever, anæmia, and starvation the free hydrochloric acid of the gastric juice is diminished, but in these states we know that the administration of chlorides is followed by their retention in the body, and it is probable that the blood in these conditions is poor in sodium and chlorine ions. Moreover, it seems probable that a chronic state of defective gastric secretion may produce a diminished alkalescence of the blood.

Gastro-intestinal fermentation plays an important part in deranged metabolism. Among the remote effects of excessive fermentation are alterations in the urine, which may become more acid than normal, contain an excess of uric acid and sometimes considerable excess of oxalic acid; moreover, volatile fatty acids, such as acetic and formic, may be detected. In many persons suffering with chronic gastritis abundance of starchy food and sugar causes fermentation, flatulence, distension, and malaise; while examination of the urine shows excessive excretion of uric acid, which can only be explained by katabolic changes in nucleo-proteids.

Putrefactive Processes in the Intestines in Relation to the Urine.—The decomposition processes carried on in the intestines by putrefactive bacteria give rise to the formation of various aromatic bodies, namely, indol, $C_6H_4\left\langle\begin{matrix} CH \\ NH \end{matrix}\right\rangle CH$; skatol, $C_6H_4\left\langle\begin{matrix} CCH_3 \\ NH \end{matrix}\right\rangle CH$, or β-methyl-indol; phenol, C_6H_5OH; and cresol, $CH_3C_6H_4OH$. Since these substances leave the body as aromatic sulphates, it is possible to determine the degree of putrefactive action by estimating the amount of aromatic sulphates as compared with the preformed sulphates in the urine. Various clinical conditions associated with catarrh of the intestines and chronic constipation often show excess of aromatic sulphates in the urine. But excess of aromatic sulphates in the urine is not always connected with putrefactive decomposition of proteid in the intestines: it may accompany excessive suppuration without free drainage, or depend on the administration of aromatic drugs, such as salol, creasote, and benzosol. It is probable that the long-continued absorption of these products of putrefaction in excess may lead to nervous disturbance, and that this is especially likely to occur in those who are potentially unstable. The well-known influence of a purge or enema in preventing fits in epileptics or general paralytics may be mentioned in support of this opinion. According to Folin a small amount of ethereal sulphates may arise from metabolic processes.

Among the chemical defences of the organism may be reckoned the *synthetic activities of cells*, as a result of which the sulphuric acid formed from the oxidation of the sulphur of proteid metabolism combines with these aromatic bodies and renders them harmless and capable of elimination by the urine in the form of ethereal sulphates. Since the

supply of sulphuric acid is not inexhaustible, it follows that when the aromatic sulphates are abundant the preformed sulphates are considerably decreased. Sometimes, indeed, the aromatic sulphates may be so excessive that all the sulphuric acid available is combined with the aromatic bodies, and the preformed sulphates (precipitated by a solution of chloride of barium) disappear from the urine. This may occur in carbolic acid poisoning. The aromatic sulphates also combine with glycuronic acid to form glycuronates.

Indicanuria.—The urine of young children is free from indican, and its constant presence in more than a minute trace therefore indicates some abnormal condition. Indol, like skatol, is a derivative of tryptophane (indol-amino-proprionic acid), a product of proteid digestion. Indol, when formed in the intestines or introduced experimentally, is rapidly absorbed and carried by the portal blood to the liver, where it is oxidised by the protoplasm of the living cells and converted into indoxyl, and subsequently, by the action of sulphuric acid and potassium salts, into indoxyl-potassium sulphate. This substance is excreted by the kidneys, and is generally called indican, since it was at first regarded as identical with the indigo of plants, because when oxidised it turns the urine an indigo blue colour. Thus:

$$\begin{array}{lllll} & \text{Indoxyl-potassium sulphate.} & & \text{Indigo blue.} & \text{Acid potassium sulphate.} \\ \text{Or} & 2 \cdot C_8H_6NOSO_3K + O_2 & = & C_{16}H_{10}N_2O_2 + & 2KHSO_4. \end{array}$$

Persistent indicanuria points to excessive putrefactive processes in the intestines, and is associated with constipation, irregular action of the bowels, flatulence, foul smelling stools, loss of weight and strength, sallow complexion, and various functional disturbances of the nervous system. It is probable that the indol is produced by the action of the Bacillus coli on proteid material. Susceptibility to the poisonous influence of indol varies in different individuals. It is only moderately toxic to man; thus small doses produce frontal headache, irritability, and restlessness, while large doses, according to Herter's experiments, may set up diarrhœa without further symptoms, or may induce a condition of marked irritability, insomnia, and mental confusion; and when enough is absorbed continuously, as shown by a constant indican reaction of the urine, neurasthenic symptoms may result. Other products of proteid putrefaction may have important effects upon the organism and lead to the production of chronic functional nervous diseases.

An example of synthetic action of the living cells is afforded by the production of hippuric acid, $CH_2NH\begin{cases} COC_6H_5 \\ COOH \end{cases}$, by the union of benzoic acid (C_6H_5COOH) with glycocoll (amido-acetic acid, CH_2NH_2COOH).

$$C_6H_5COOH + CH_2 . NH_2COOH = CH_2NH\begin{cases} COC_6H_5 \\ COOH \end{cases} + H_2O.$$

Hippuric acid is a normal constituent of the urine, and is derived from the benzoic acid contained in vegetable food, but is partly also, according to Baumann, a product of intestinal putrefaction.

The sulphur in proteids is mainly present as a cystin radical, and another result of proteid putrefaction is the production of simple sulphur compounds, among which may be mentioned sulphuretted hydrogen and methyl-mercaptan (CH_3SH). These sulphur compounds are normally produced in small quantities in the large intestine, but excessive putrefaction of sulphur-containing proteids may in rare instances, as in Senator's case, be associated with the appearance of sulphuretted hydrogen in the urine (*hydrothionuria*) and nervous symptoms.

Exceptional Forms of Intestinal Putrefaction associated with Appearance of Abnormal Constituents in the Urine.—*Cystinuria.*—

Cystin, $S_2\left\langle\begin{array}{l}C(CH_3)NH_2COOH\\ C(CH_3)NH_2COOH\end{array}\right.$, is slightly soluble in the urine, and separates out in the sediment in the form of colourless hexagonal crystals. It is insoluble in water and alcohol, but dissolves in mineral acids and alkalis. A trace of nitro-prussiate of sodium added to an alkaline solution of cystin gives a violet coloration. Cystinuria is of some clinical importance, because calculi, consisting largely of cystin, are occasionally formed; but it is also of interest because it is frequently associated with disordered digestion, anæmia, and putrefactive processes in the intestine. Further, cystinuria is sometimes hereditary. The existence of cystinuria is constantly, if not absolutely regularly, associated with the excretion of putrescin $\left(\text{tetra-methylene-diamine, } \begin{array}{l}CH_2CH_2NH_2\\ \mid\\ CH_2CH_2NH_2\end{array}\right)$ and cadaverin $\left(\text{penta-methylene-diamine, } \begin{array}{l}CH_2CH_2NH_2\\ \mid\\ CH_2\\ \mid\\ CH_2CH_2NH_2\end{array}\right)$. As these bodies are undoubtedly the result of bacterial action upon proteids, and the only explanation of their appearance in the urine and fæces is that they originate from putrefactive processes in the intestines, it might be surmised that the concomitant cystin in the urine had a like origin. Another explanation, however, is that cystin is an intermediate product of metabolism, which is ordinarily broken up with oxidation of the greater part of its sulphur to sulphuric acid; it may be urged in support of this view that there is no evidence to show that cystin itself is a product of putrefaction.

Alkaptonuria.—Alkapton or homogentisic acid $\left(\text{di-oxy-phenyl-acetic acid, } C_6H_3\begin{array}{l}\diagup OH\\ -OH\\ \diagdown CH_2COOH\end{array}\right)$ has in rare instances been found in the urine. These urines on exposure to the air, or on addition of alkali, turn brown

on the surface and even become black. Alkaptonuric urine reduces Fehling's solution, but it differs from urine containing sugar in not giving the fermentation test, in not reducing alkaline bismuth solutions, and in not rotating polarised light. Alkaptonuria is a "freak of metabolism" which frequently shows itself in several members of a family; although there is no recorded instance of the parents having manifested alkaptonuria, it is nevertheless quite possible that consanguinity plays a part, for Dr. Garrod has shown that eleven cases, belonging to four families, were children of first cousins. It may begin after the first meal at the mother's breast and persist during life without any apparent detriment to health. Dr. Garrod supports the view that the change from tyrosin to homogentisic acid takes place in the tissues after the absorption of the former rather than the alternative view that the change in question is brought about in the alimentary canal.

Lecithins, which are present in many articles of food, especially in yolk of egg, may possibly undergo decomposition and cause the formation of toxic products cholin and neurin; for further information concerning these bodies and their toxic actions *vide* p. 579.

Headache, drowsiness, and mental depression show that toxic products of intestinal putrefaction are no longer being adequately dealt with by the living tissues of the alimentary canal and liver, and are finding their way into the systemic circulation. The immediate relief afforded by a free evacuation of the bowels by a dose of calomel suggests that the power of the liver to deal with the toxins produced in the alimentary canal has been restored.

Glycosuria.—This subject is fully discussed elsewhere (see article "Diabetes," vol. iii.), but a few remarks here may not be out of place, as glycosuria is essentially *a disorder of carbohydrate metabolism* in which sugar accumulates in the blood, because the cells of the body, which normally obtain a great amount of heat and energy from its oxidation, are unable to make use of the sugar in this way. This inability may be explained as follows: (1) defective oxidation of the sugar by the cells of the body; (2) defective splitting up of the sugar molecule; (3) defective storage of glycogen; (4) sugar accumulates in the blood by an impairment or failure of the vital activities of the protoplasm of the cells lining the alimentary canal, and of the liver to utilise sugar in the formation of fat and proteid or to transform the same into glycogen (Pavy). There is no evidence to show that the oxidation-capacity of the cells is diminished in diabetes; for the products of proteid metabolism, urea and uric acid, are approximately normal and the fats are oxidised as in health to carbon dioxide and water. Again, in some cases of diabetes, lævulose, a lævo-rotatory sugar, is utilised in the organism. Moreover, in many diseases in which there is deficient oxygenation of the blood, sugar does not appear in the urine; nor does it in phosphorus poisoning, in which the capacity of oxidation by the cells of the body is much reduced.

It is probable that the condition of *hyperglycæmia* arises from an inability to prepare the sugar for oxidation by splitting its molecule into

simpler molecules. Glycuronic acid, $COOH(CHOH)_4COH$, is a derivative of sugar, and is perhaps the first stage in the process of the splitting of sugar into simpler molecules; it is closely related to glucose, from which it differs by the replacement of two atoms of hydrogen by one of oxygen. This process of oxidation is readily brought about in the normal organism, and there is experimental evidence that this oxidation process occurs even in severe cases of diabetes. Hyperglycæmia may therefore depend on the cells of the body having lost their power of splitting the glucose or glycuronic acid molecule into the final products of combustion—carbon dioxide and water; in other words, the disruption of the links holding the carbon atoms together does not occur; it is possible that this separation can only be brought about by the ferment of the internal secretion of the pancreas. Certain it is that the destruction of the pancreas, experimentally in animals or by disease in human beings, is followed by continuous glycosuria.

Numerous facts, established experimentally and in other ways, show that glycosuria may have other modes of origin: *e.g.* (1) Puncture of the floor of the 4th ventricle produces glycosuria, provided there is glycogen in the liver; but if there is no glycogen, as in a starved animal, no sugar appears in the urine. The injury of the floor of the 4th ventricle interferes, then, with the glycogenic function of the liver; it is supposed that it induces dilatation of the hepatic artery, and that thus some ferment-body is brought in excess to the liver cells, and, acting on the stored-up glycogen contained in them, converts it into sugar. (2) Certain toxic substances, such as phosphorus, arsenic, carbon monoxide, morphine, hydrocyanic acid, turpentine, chloroform, phosphoric, lactic, and hydrochloric acids, cause glucose and especially glycuronates to appear in the urine.

The Relationship of Uric Acid and Urates to disordered Metabolism is of great interest, especially in connexion with gout. Uric acid, the average daily excretion of which is about 0·8 gramme, arises from the breaking down of nuclein and nucleo-proteid in the tissues, and more directly by the oxidation of such substances contained in the food. Belonging to the same group as uric acid are hypoxanthin, xanthin, guanin, and adenin. These bodies are called purin bodies, and are liberated during the digestion of the nucleo-proteids contained in food, as in the following table (Horbaczewski, after Prof. Sidney Martin):—

Nuclein or nucleo-proteid

Proteid. Nucleic acid.

Phosphoric acid.
$C_5H_4N_4 - NH$. Adenin.
$C_5H_4N_4O - NH$. Guanin.
$C_5H_4N_4O$. Hypoxanthin.
$C_5H_4N_4O_2$. Xanthin.
$C_5H_4N_4O_3$. Uric acid.

It has been found that a diet of flesh, especially veal, liver, pancreas,

and sweet-bread, containing a large amount of nucleo-proteid, leads to an increase in the excretion of purin bodies in the urine, as compared with a diet of eggs, butter, milk, fruit, vegetables, cheese, and bread. In new-born infants the amount of uric acid excreted is in excess as compared with the adult; this is no doubt due to the fact that katabolism causes a breaking down of more nucleo-proteid of the tissues and blood. The morbid conditions in which the uric acid passed in the urine is increased are leucocytosis and leukæmia; this increase may be attributed to the degeneration of the excess of leucocytes in the blood. Certain drugs increase the amount of uric acid, *e.g.* pilocarpine and salicylates. The amount of uric acid is diminished by rest and chronic gout. Uric acid does not exist as such in normal urine, but is combined with alkalis probably in the form of the more soluble quadriurates of potassium, sodium, and ammonium. The biurates are less soluble, and it is in this form, especially as the sodium salt, that uric acid is deposited in the tissues in gout; for further particulars the reader is referred elsewhere (article "Gout," vol. iii.).

Nutritional Interdependence of Organs and Internal Secretions. — There is yet another cause of defect of nutrition due to alteration of the blood, which lies in *the interdependence of each and all of the tissues of the body upon one another.* No part can be removed without some effect upon the rest of the body. We may note, for example, the profound effect on nutrition and on the male character produced by early castration; and various other organs have been shown to exercise a very considerable influence upon the blood and tissues by acts complementary to their special functional activity. I refer to those **glands** believed to have an **internal secretion** passing into the blood and playing an important part in metabolism; and I shall now consider certain of these functions.

I. *The Liver.*—Minkowski has shown that, after extirpation of the liver in birds, uric acid is in great part replaced by ammonia and lactic acid. It is impossible to extirpate the liver in warm-blooded animals; but Murchison always taught that nitrogenous waste products of tissue-metabolism were converted by the liver into urea. We know that amino-acids are formed in the intestine out of proteid, and that animals fed on leucin and other amino-acids excrete an increased quantity of urea. It cannot be supposed that leucin becomes an integral part of the liver cells; but it undergoes chemical changes, the ultimate product of which is urea. Hence when the liver undergoes destruction, as in acute yellow atrophy, leucin and tyrosin appear in the urine. There is not the slightest doubt that urea is far less poisonous than its antecedents; moreover, urea favours urinary secretion, and may be considered a physiological diuretic. The experiments of Hahn, Nasse, Pawlow, and Nencki have shown that in dogs carbamate of ammonia may be made to accumulate in the urine, that it is highly poisonous, and that it arises from tissue-metabolism and disintegration. They also found that the injection of sodium carbamate into the circulation of dogs was poisonous

only to those animals in which the portal current had been diverted into the vena cava, the portal vein ligatured, and the liver thus thrown out of action (fistula of Eck). This suggests that the carbamate of ammonia is converted into urea by the liver. When the hepatic artery is simultaneously ligatured there is a great increase of carbamate of ammonia. It has been shown that small quantities of this salt exist in the blood, and animals in which the liver is normal suffer no ill effects from its injection; whereas those in which the liver has been put out of action die of peculiar nervous phenomena. These observers think the intoxication of the organism by the products of cellular activity is a complex process, and that their experiments show that one function of the liver is to destroy and transform poisons arising in the organism from cellular activity. Their long series of experiments indicate that the liver protects the organism from poisoning by the products of its own cellular activity; and they make it probable that certain complications arising in hepatic insufficiency of various kinds are due to carbamate of ammonia. It is probable, however, that this is one only of many nitrogenous antecedents of urea.

The liver, again, standing as a safeguard between the portal and general circulations, protects the body from the influence of toxic substances produced by the alimentary canal or taken into it. The researches of Bouchard have proved that, for the same quantity of nitrogen, urea is forty times less poisonous than ammoniacal salts; and in his work on *Auto-intoxication* he has demonstrated that this function of the liver diminishes in an enormous proportion the toxicity of the waste products.

II. *The Pancreas.*—Researches and clinical observations have shown that this organ, besides its digestive functions, discharges into the blood certain products without which the organism is incapable of utilising the glucose normally contained in the blood; hence this accumulates and gives rise to glycosuria or pancreatic diabetes. Von Mering and Minkowski have proved that animals from which the pancreas has been completely extirpated become glycosuric. Lancereaux and other clinicians had previously called attention to lesions of the pancreas in association with diabetes. But the trouble does not seem to come from the accumulation in the organism of a poisonous substance, for no effect is produced on a healthy dog by injecting into its system the blood of an animal which has become diabetic by extirpation of the pancreas. Gley succeeded in tying all the veins of the pancreas and produced glycosuria; and other experiments seem to show that the pancreas has normally a function of elaborating and turning into the blood a glycolytic ferment, necessary to enable the tissues to utilise the sugar contained in it. Complete extirpation of the pancreas is necessary in order that the sugar may thus accumulate in the blood.

III. *The Thyroid Body.*—As early as 1856 Schiff proved that dogs, in which he had completely extirpated the thyroid gland, presented numerous disorders and alterations of nutrition analogous to those

observed in man after thyroidectomy. He put forward the hypothesis that the thyroid elaborated a substance which passed into the circulation and played an important part in the nutrition of the nervous system. This has since been verified experimentally and clinically. (*Vide* art. "Myxœdema," vol. iv.)

IV. *The Pituitary Body.*—Experiments have shown that when the gland is removed in animals tremors and spasms occur. No result follows injection of extracts of the anterior lobe into animals, but extracts of the posterior lobe produce alterations of blood pressure owing to the presence of two substances, one of which produces a rise, the other a fall. (*Vide* article "Acromegaly.")

V. *The Suprarenal Capsules.*—Addison pointed out a peculiar pigmentation of the skin associated with caseous degeneration of these glands. Brown-Séquard has shown that extirpation caused great disturbances of nutrition, often followed by death. In all cases of ablation of these organs there is accumulation of pigment in the blood, and also, according to the researches of Abelous and Langlois, of poisonous products of unknown nature. Prof. Schäfer and Dr. G. Oliver showed that injection of suprarenal extract into the circulation of animals is followed by an enormous rise of blood pressure. They came to the conclusion that the medullary portion of the gland secretes a material which increases the tone of all muscular tissue, especially of the heart and arteries. The active material is a methylamine derivative of pyrocatechin, generally termed adrenalin.

Dr. Bradford's experiments also show that *the kidneys*, besides the functions of elimination of waste products, possess another concerned with the metabolism of the tissues. (*Vide* art. "Gen. Path. of the Kidneys.") *The spleen*, in contradistinction to the above-mentioned organs, can be removed without producing any notable physiological effect beyond compensatory hypertrophy of the lymphatic glands.

Influence of the Nervous System upon Nutrition.—The influence of the mind upon the nutrition of the body is well known: anxiety, mental strain, with associated insomnia, are followed by lowered nutrition and general wasting of the body. Many neuroses—such as neurasthenia, hysteria, epilepsy, and various forms of insanity—are associated with failure of nutrition and general wasting of the body; and this condition also obtains in certain cases of nervous exhaustion in highly intellectual persons. Improvement of the nutrition of the body is often followed by improvement of the mental state, as in mania, melancholia, hysteria, and neurasthenia.

The question before us, however, is not whether derangement of the nervous system may prevent assimilation, but whether the nervous system exercises a direct trophic influence upon the tissues? We have undoubted proof within the nervous system that nerve-cells exercise a trophic influence upon nerve-fibres; but are there nerve-fibres which can modify the "nutritive exchanges" of the cells independently of the vascular or other known changes? In reply I shall treat of the experimental data,

reserving clinical incidents for the sections on "Necrosis," "Atrophy," and "Hypertrophy."

Intracranial section of the fifth nerve produces inflammation of the eye, ulceration of the cornea, and suppuration and destruction of the eyeball of the same side; but it is asserted that these accidents do not occur if the eyelids are sewn together, and the delicate surfaces of the conjunctiva and cornea thus protected from the injury of foreign bodies, especially microbes.[1] This argument is invalidated, however, by the observation that in paralysis of the seventh nerve the eyeball is much more exposed and yet no trophic disorders follow.

Section of the cervical sympathetic is said to produce in a young rabbit an increased growth of the ear; section of the facial nerve to produce an increase in size of the maxillary bones: doubtless in both cases the results are due to increased vascularity, and consequent increased nutrition of those parts.

Section of the anterior roots or motor nerves offers perhaps the best evidence of trophic influence, for the wasting of the muscles is then much more rapid and extensive than disuse of the muscles would produce; and it is attended by electrical changes with the "reaction of degeneration." Certainly the assumption of a direct trophic influence of the nervous system upon the cells and tissues of the body helps us to explain many important clinical phenomena; but it cannot be asserted that the clinical facts afford indisputable proof of the existence of independent trophic nerve-fibres.

The Acquired or Inherited Specific Properties of the Blood and Tissues.—On the failure of nutrition in wasting diseases such as phthisis, cancer, infectious diseases, the reader is referred to special articles; so also on the effects of poisons such as lead, alcohol, and phosphorus.

The "*durability of life*" of the cells of each and all the tissues of the body depends largely upon specific inherited properties of longevity. It may happen that all the organs of the body possess an inherited longevity, that if environment be favourable all the tissues will pass through all the stages of growth and natural decay, terminating in gradual dissolution; and the organism pass out of the world as unconscious of death as of birth. On the other hand, there may be an inherited defect in the "make-up" of one particular tissue, rendering it susceptible to disease and degeneration. Should such a tissue be endowed with an important function which cannot be assumed by another tissue, then the whole of the tissues of the body would suffer either from the effects of mal-assimilation or non-removal of the waste products; and

[1] Professors Goltz and Ewald showed (at the International Physiological Congress held at Berne, 1895) a dog in which the spinal cord from the last cervical segment downwards had been removed. The muscles of the bladder and rectum preserved their tonus, and there were no trophic changes in the skin, hair, and nails; but of course all the striped muscles of the lower limbs had completely wasted. Inasmuch as the spinal ganglia and sympathetic ganglia had not been destroyed, it may be inferred that the absence of changes in the skin and appendages depended upon integrity of the former, and the preservation of the smooth muscle-fibres of the viscera on the integrity of the latter.

the local disease would then cause a derangement of nutrition of the whole organism and perhaps a general dissolution.

Progressive and General Failure of Nutrition

General arrest of nutrition of the tissues of the body will produce *somatic death.* General wasting or inanition may arise from diseases such as cancer or stricture of the œsophagus; destruction of the mucous membrane of the stomach by corrosive fluids or disease; uncontrollable vomiting and hysterical anorexia; pressure of growths upon the thoracic duct; cancer of the pyloric end of the stomach, and cancer of the pancreas. Whether cancer produces its characteristic cachexia by interfering with digestion and assimilation, or whether some products escape from the growth into the blood, or some substance is taken from the blood by the growth, thus altering its composition, is at present a matter of speculation; but certainly the sarcomas, which are of mesoblastic origin, do not produce the same marked effect upon nutrition as carcinomas. There are a number of diseases which produce general wasting by increased destructive metabolism accompanied by fever, by hæmorrhages, or by exhaustive discharges from the body, in none of which the process of repair is adequate, and a progressive failure of nutrition ensues; such are fevers, phthisis, diabetes, prolonged suppuration, dysentery, and albuminuria. General wasting from exhausting diseases is always attended by a certain amount of tissue metamorphosis and degeneration, as in coagulation-necrosis, hyaline degeneration, fatty and lardaceous change,—the location of the tissue-change depending upon the nature of the disease and the ability of the organ or tissue under abnormal conditions of nutrition to maintain the equilibrium between repair and waste.

In general wasting of the body from starvation the various tissues are affected unequally: 97 per cent of the fat is lost, 30 per cent of the muscle, 28 per cent of the blood, and of the heart only 2 per cent. Wilks and Moxon point out that in cancer the heart usually wastes very much, in one case being reduced to 4 oz.; whereas in phthisis it does not atrophy, although there may be extreme emaciation of the body. Perhaps in the former it is partly disuse-atrophy, owing to the progressive diminution of the amount of blood and tissue.

In old age there is a gradual wasting of all the tissues of the body (the heart sometimes excepted). There may be a *simple atrophy of cell-elements* without structural modification, due to a lowering of the vital activities of all the tissues, or *various degenerative* processes common to senile decay.

Retrogressive Disturbances of Nutrition

A. **Necrosis or Tissue-Death.**—Necrosis of a tissue may be partial or complete. The essential or specialised cells of an organ or tissue may die, while the mechanical supporting tissues remain and undergo

proliferation. Since the former cannot regenerate, the latter fill up the gap. If tissue-death or necrosis occur in situations favourable to the presence or introduction of micro-organisms, then we have no longer an aseptic, but a septic necrosis, or gangrene; of this there are two varieties, moist or spreading, and dry. In the former the conditions are favourable to the growth and spread of the putrefactive microbes, in the latter they are not; hence the process is usually limited by a "line of demarcation."

Causes and Pathogeny

Traumatic.—(1) Mechanical injury, such as violent contusions or tight bandaging; (2) Heat and cold; (3) Chemical, such as strong corrosives, acid or alkaline; (4) Electricity. These causes produce complete death of the tissue as a rule, and are, at any rate at the onset, aseptic.

Mechanical injury produces death of the tissue by inducing blood stasis, and by its direct effect upon the tissue-elements.

Heat produces death by coagulation; several very important albuminous substances, *e.g.* myosinogen and fibrinogen, are coagulated at 56° C. This would indicate that the tissues and fluids of the body exposed to this temperature would solidify, and thus inevitably be killed.

Hyperthermia of the Body.—A very high temperature of the body is incompatible with life. Experimental hyperthermia in mammals shows that a temperature of 47° C. is immediately fatal; a temperature of 45° C. kills in an hour or two; a temperature of 43° C. kills after a longer lapse of time. Professor Halliburton and I have shown that the fatal temperature of 47° C. coincides with the coagulation-temperature of neuro-globulin. But we found that prolonged heating even at 42-43° C. produced coagulation of a solution of neuro-globulin. Moreover, these facts can be correlated with definite histological changes in the nerve-cells (*vide* Plate V. Figs. 2 and 3). We therefore came to the conclusions—(1) that when this constituent of cell-protoplasm is coagulated the protoplasm loses its vitality; and (2) that the coagulation of the cell-globulin is the physico-chemical cause of death in hyperpyrexia.

Temperatures below 16-18° C. destroy living protoplasm; the nature of the tissue and the period of time to which it is exposed to abnormal conditions of temperature will determine whether it can be restored to functional activity.

Corrosive Fluids.—Strong acids produce immediate death by *coagulation* of the blood and tissues. Strong *alkalis* disorganise the tissues by *liquefaction*, producing a soft eschar.

Electrolysis.—At the negative pole the eschar is soft and resembles the destruction produced by alkalis, whereas at the positive pole the eschar is dry, yellowish, and similar to the effect produced by acids (*vide* p. 436).

B. **Necrosis by Disturbance of the Circulation.**—All causes which bring about *stasis* of the blood in the capillaries, such as inflammation,

pressure, hæmorrhage, or blocking of the venous outflow of a part, will cause necrosis by arrest of nutrition. Again, if the arterial supply of a part be cut off by ligature, embolism, thrombosis, or slow degeneration and obliteration of the vessel, anæmic necrosis results. The arrest of the circulation need not be permanent; it suffices if it persist a certain time. The more highly specialised a tissue the briefer its vitality when deprived of blood. The grey matter of the central nervous system, the epithelium of the intestine and the kidneys, can live but a short time (one to two hours, Cohnheim) without their blood-supply. So if one of the above causes should lead to anæmia of a specialised tissue, death of the specialised cell-elements has generally occurred before the circulation can be re-established. This is particularly liable to happen in organs having terminal arteries. (*Vide* art. "Embolism.") Direct injury, if severe, produces tissue-necrosis by complete arrest of nutrition of a part; but those remoter causes which consist in the weak defence of the organism against injury, although subsidiary, are quite as important. Thus comparatively trivial immediate causes may produce a spreading necrosis and circulatory disturbances of nutrition, which in a healthy individual could easily be overcome. The predisposing causes are:—

(*a*) *Disturbances of Innervation.*—We have argued that division of the fifth nerve proves no more than that the loss of innervation of the cornea causes sloughing, by abolishing the reflex defensive mechanism of the tissue against microbes. Section of the posterior roots in monkeys produces sores upon the feet, but section of an equal number of roots supplying the upper limb produces no sores upon the hands; the hand is not subjected to the same direct injurious influences of pressure and microbic infection. Charcot maintained that acute bed-sore occurring upon the buttock of the paralysed side in some cases of apoplectic hemiplegia was a proof of the existence of direct trophic influence. He stated that when certain patients had only lain on the non-paralysed side, and every precaution had been taken about the urine and fæces, yet within some hours or days a purplish erythematous rash might appear, and bullæ form and burst, leaving a red, sore surface followed by an eschar and usually by sloughing out of the mortified part. Local infection may then ensue and become general. In acute myelitis the bed-sores occur over the sacrum and heels. Déjérine and Leloir, also Pitres and Vaillard, have shown that changes in the peripheral nerves often occur in cases of hemiplegia with acute bed-sores.

Trophic changes occur in Morvan's disease and syringomyelia; of the former painless whitlows are an essential feature. The perforating ulcer of locomotor ataxy is another example of tissue-necrosis due to changes in the peripheral sensory nerves. Dr. Head has shown that herpes zoster is due to inflammation of the posterior root ganglion. Whatever view be taken of the existence of trophic nerves, the important fact remains that disturbances of the normal nervous influences, vasomotor and sensory, directly modify the nutrition of the parts, and interfere with the defensive action of the organism against microbic invasion.

Raynaud's disease is a local asphyxia which is often followed by symmetrical dry gangrene of the extremities. The observer after whom the disease is named considered it to be due to constriction of the small arteries owing to vasomotor spasm. A number of cases, however, have been brought forward showing endarteritis obliterans. (*Vide* art. "Raynaud's Disease.") It is possible also that acute perforating ulcer of the stomach may be induced by reflex vasomotor spasm.

(*b*) *Lowered Vitality of the Tissues.*—Age is relative; the vital reaction of cells is partially dependent upon inherited specific properties and partially upon present conditions of nutrition. Premature decay of tissue may be inherited or acquired, and death ensues as soon as the vital energy is unable to cope with the antagonistic influences of its environment. Senile decay and death, however, come sooner or later to the healthiest tissues in the most favourable surroundings; it comes when the original vital capacity is exhausted, when the mainspring of life is worn out. Whether, then, the lowered vitality of the tissues be premature or natural, the tendency to necrosis and gangrene is much greater when an immediate cause exists, such as direct injury or disturbance of nutrition. Many diseases are specially liable to be followed by gangrene and bed-sores. Gangrene of the scrotum, penis, and even of the nose, has been known to occur in cholera (Fagge). In typhoid fever, Liebermeister points out that gangrene and necrosis of bone my occur; chancres may lead to spreading gangrene, and gonorrhœa to sloughing of the penis. Bed-sores are very apt to arise even during convalescence. During and following typhus fever gangrene is not infrequent, and noma of the cheek and vulva is not unknown after measles. Gangrenous dermatitis occasionally occurs in ill-nourished, tuberculous, or syphilitic children. (*Vide* arts. "Varicella," "Vaccinia.") All these consequences are due to lowered vital resistance engendered by the disease, to lowered defence of the tissues against microbic infection and multiplication, so that microbes gaining entrance to the tissue find a suitable soil for development.

The entrance of certain poisons into the blood—*e.g.* ergot of rye, anthrax, snake poison, plague micro-organisms—is followed by necrosis. With regard to ergot it has been supposed that this is due to constriction of the small arterioles by the poison; but instead of the arterial pressure being increased, it is diminished. No doubt many factors are at work in the gangrene of ergotism.

Secondary Gangrenes.—The presence of gangrene in one part of the body may be followed by *secondary foci* elsewhere. They generally appear in the lung and depend on embolism. It is obvious that the parts most open to infection by the microbes present in the environment are most liable to a gangrenous inflammation. Therefore gangrene especially occurs when the parts affected are in relation to the alimentary canal, the respiratory tract, and the external skin. It only occurs in the nervous system in cases where profound infective ulceration has penetrated the dura mater. It hardly ever occurs in the liver, spleen, kidneys, or bones: it generally spreads, but its progress may be

arrested by antiseptics and the actual cautery. Eschars produced by physical or chemical agents in healthy people do not spread, as a rule, because the tissues are destroyed or form an unsuitable soil for the development of micro-organisms.

Morbid Anatomy and Pathology of the Different Forms of Necrosis

1. **Coagulation-Necrosis.**—Weigert has shown that when a part of the body rich in protoplasm dies, it usually undergoes coagulation-necrosis. In order that coagulation may take place a coagulable material must be present. In all parenchymatous tissues, except the brain, the intercellular fluid is coagulable lymph. When cells die from arrest of nutrition, as in embolism and thrombosis, the first evidence of death is a change in the appearance of the nucleus and chromatic substance: when the organ has been washed free from blood by normal saline solution there are practically no naked-eye appearances of a recent infarct; but examined microscopically it is found that the cells or cellular structures do not stain with hæmatoxylin, and that the nuclei have either altered in appearance or disappeared. Professor Halliburton has shown that he can prepare from many tissues a nucleo-albuminous substance, which rapidly brings about coagulation of blood or lymph. The cells deprived of nutrition die, liberating a nucleo-albuminous material, and this reacting upon the coagulable lymph that has penetrated from without produces a coagulation within the cell. Cohnheim, who gave the name of coagulation-necrosis to this necrotic change, considered it to be due to the interaction of the fibrino-plastin and fibrinogen. The process of arrest of nutrition must not be too protracted, or degenerative processes, such as *fatty change*, may ensue and render the process of coagulation impossible. The protoplasm of the cells which have undergone coagulation-necrosis somewhat resembles coagulated fibrin in appearance. Often small, transparent, hyaline masses are seen, and sometimes the cells have a homogeneous appearance. The nucleus may be indistinct, absent, swollen up, finely granular, or confused with the contents of the cell. Later the products of necrosis disintegrate and are absorbed. According to Weigert, these appearances are found in white infarcts, atheroma, caseous degeneration of tumours and glands, waxy degeneration of muscle, and the superficial necrosis of the tissues in diphtheria.

Waxy degeneration of muscle (Zenker) is an example of coagulation-necrosis. After death muscle-fibre invariably coagulates, but preserves its striation. Under various pathological conditions, such as continued fever, certain muscles (*e.g.* rectus abdominis) undergo a peculiar change. To the naked eye the fibres appear dull and semi-opaque: microscopically they are found to have lost their striated appearance, the contents of the sarcolemma are broken up into lustrous homogeneous lumps, and between the fibres there is a proliferation of the connective-tissue cells.

2. **Colliquative Necrosis.**—Sometimes the dead tissue-elements are infiltrated with a serous effusion, and then undergo liquefaction. In a burn the cells are killed by the action of the heat, and with them the ferment that would produce coagulation of the transudation of the blood. The dead cells absorb the fluid and swell up, forming a vesicle; or, if the blood be coagulated in the vessels, non-coagulable serum will escape and produce liquefaction of the tissues. Colliquation may follow upon coagulation. In croupous pneumonia the liquefaction of the coagulated products is probably due to the action of ferments (autolysis). Thrombi also break down and liquefy. In the brain colliquative necrosis occurs as the result of vascular occlusion; the tissues undergo softening and are rapidly destroyed. The cerebro-spinal fluid, which probably represents the lymph of the central nervous system, is a non-coagulable fluid. Hence liquefaction instead of coagulation of the tissues results, and the final part of the process may be the formation of a cyst or cicatrix.

3. **Caseation** or **Tyrosis** is a mode of termination of necrosis.

4. **Gangrene** or **Infective Necrosis**, of whatever form, is preceded or accompanied by abnormal sensations in the part. It may be coldness or a dull aching, not infrequently severely lancinating or burning. When the integument is involved the pain is more intense, and when an internal organ is affected it may be absent.

Varieties of Gangrene.—Dry—or Mummification.—Spontaneous gangrene is very liable to occur in old people with atheromatous or calcified arteries. It is limited in extent and chronic in progress. Several causes usually combine to bring about the morbid process: *e.g.* an enfeebled circulation, due to cardiac failure, in a remote and dependent part of the body, as the toes or foot, rarely the fingers; or the diseased condition of the arterial wall, by which a gradually extending thrombosis is favoured. The thrombus may extend as far as the popliteal artery, and yet the gangrene be limited to the toes or a portion of the foot. Stasis in the arteries and capillaries of the part, due to feebleness of propulsion, produces the gangrene; and this stasis may be determined by slight injury or abrasion, the cutting of a corn, or any such cause of local inflammation. Putrefactive organisms may be present in the skin, but they require moisture to develop in the tissues: this they do not get, because it evaporates from the surface, especially when the skin separates and peels off. As putrefaction cannot take place there is little or no odour in this form of gangrene. Frost-bite and ergotism lead to mummification, and a physiological example of the process is the necrosis of the umbilical cord. The affected part is generally livid, owing to the contained blood, and the changes in colour are due to its alteration: it becomes withered, black, and dry because no more fluid reaches the part, and the remainder evaporates. An inflammatory zone—the line of demarcation—separates the dead part from the healthy. Occasionally dry gangrene may go on to *moist gangrene*; the latter is a necrosis accompanied by putrefaction, and is especially apt to occur in situations which

are in direct or in indirect communication with the air, *e.g.* in the lungs, the alimentary canal, or the integuments. When septic micro-organisms reach a necrotic part rich in blood, or other fluid, decomposition rapidly sets in, and changes occur in the colour of the part, which assumes a bluish, livid appearance; the epidermis is frequently raised into bullæ and blebs, and a very foul odour arises, due to the formation of various gases, which sometimes produce emphysema.

One form of gangrene, *the acute spreading*, is due to a specific micro-organism. The tissues undergo destruction unequally: the blood and softer tissues are first broken up; and, if examined microscopically, broken-up blood-corpuscles are found, colouring the part, and undergoing transformation into granular pigmentary derivatives of hæmoglobin. The cell-nuclei disappear, and the protoplasm is turbid and breaking up into granules. Muscle-fibres lose their striation, and the sarcolemma contains only fatty and granular matters. The connective-tissue fibres, owing to the swelling up of the interfibrillary substance, break up into their primitive fibrillæ. Nerves, owing to their fibrous tissue-sheaths, resist dissolution much longer than muscles; but the nerve-fibres themselves at a very early period undergo changes in the myelin sheath similar to degeneration. Among the chemical products of decomposition are large quantities of fat which arise even in tissues where there is no fat, such as the lung. Fatty acids—caproic, caprylic, butyric, valerianic—are formed, to which, and to ammonium sulphide and hydrogen sulphide, the foul odour is in great measure due. Microscopic examination of the dirty grey, greyish black, or yellowish grey semi-fluid mass into which the tissues are eventually changed may show crystals of tyrosin, leucin balls, characteristic needles of margarine, and triple phosphates with granules of black or brown pigment. Virchow has shown that a rosy colour can be obtained by the action of nitric acid upon a gangrenous part—the "erythroproteid reaction." Unless surgery intervene, the powers of the individual to cope with moist gangrene are insufficient; the organisms are diffused by the lymphatics, and finding a suitable soil with warmth and moisture, they grow more rapidly than they can be destroyed.

IMPAIRED NUTRITION.[1]—It has been shown that permanent arrest of nutrition causes cessation of function and death of a tissue. We have now to consider those morbid processes in which impairment of nutrition and a proportional diminution of function ensue. "A cell is not nourished, but nourishes itself." Tissues will, therefore, undergo **atrophy** or **degeneration** when their component cells are unable to maintain equilibrium between repair and waste. The main factors of impaired nutrition of tissues are—

1. *Absence or recession of the normal physiological stimulus.*

2. *Inherent defect of the cell-elements to nourish themselves, therefore premature decay.*

[1] For the effect upon nutrition of inflammatory processes, *vide* article "Inflammation": in which also atrophic processes arising from inflammatory action are dealt with.

3. *Deficiency in the quality or quantity of the blood and lymph-supply.*

Any of these factors, singly or combined, may lead to a rapid or gradual retrogressive change of the tissue-elements terminating in atrophy and degeneration (both stages towards death); and in some cases the nutritional changes are so extreme that death of the tissue-elements does occur. Morbid retrogressive nutritional changes occurring in the master tissues—glandular, muscular, or nervous—and in the vessels must of necessity be progressive and cumulative, and sooner or later lead to somatic death.

Several abnormal products may arise in the tissues as the result of impaired nutrition. These substances may originate within the cell-elements of the tissue from the destructive metabolism of its protoplasm, or be brought by the blood and deposited in the tissue; thus the processes of degeneration are divided into two groups—*metamorphoses*, or degenerations proper, and *infiltrations*. The two conditions are often associated, and to draw a hard and fast line between them is difficult.

The **metamorphoses** are mucoid, hyaline, colloid, lardaceous or amyloid, and fatty. The normal metabolism of the cell is altered, resulting in chemical and histological changes of its protoplasm, and the metamorphosis may continue until the cell is entirely destroyed. In the earlier stages function is impaired, and in the later stages it may be completely arrested.

The **infiltrations** are fatty, calcareous, and pigmentary; the new material is not a product of the cell-protoplasm, but a deposition from the blood. Since the change is not usually accompanied by destruction of the histological elements, the structure and function of the tissues are much less altered than in the metamorphoses.

ATROPHY AND FIBROSIS.—The various examples of arrested development—such as microcephaly, anencephaly, amyelia, and congenital malformations—are not, properly speaking, atrophic processes due to impaired nutrition, but rather to an inherited developmental defect; so that to them the term *Agenesis* is more appropriate. The peculiar condition termed by Virchow *Hypoplasia* or *Aplasia*, observed frequently in chlorotic girls, is associated with imperfect development of the aorta and larger arteries, accompanied by a remarkable degree of elasticity. The heart is frequently dilated and the left ventricle hypertrophied. These cardiovascular conditions are associated with imperfect development of the uterus and genital organs.

Atrophy from absence or recession of the normal physiological stimulus.—There are many examples of physiological *disuse-atrophies*, *e.g.* of the ductus arteriosus, the ductus venosus, the thymus gland, and the involution of the gravid uterus after parturition. Nutrition and functional activity are interdependent, the two falling off together. The muscles and glands offer excellent examples of tissues which undergo atrophy from disuse; and bones likewise which no longer subserve the statical purposes of the organism—a familiar example of which is the wasting of the alveolar portion of toothless jaws. An example of disuse-atrophy in

the viscera is afforded after left lumbar colotomy by the dwindling of the distal part of the large bowel to a scarcely pervious cord.

Cohnheim states—"Nor is it all-important whether the failure of a muscle to contract or of a gland to secrete be caused by defective innervation or by occlusion of its duct." He attributes the greatest share in the atrophy to the abeyance of functions. No doubt the falling off in volume of the thigh muscles which occurs in ankylosis of the knee-joint is very great, but experiments upon animals made by Prof. Sherrington and myself lead us to believe that the atrophy of the muscles and reaction of degeneration which occur in infantile paralysis are something more than the effect of disuse; and that the muscles depend for their nutrition upon a physiological stimulus which is continually passing from the anterior horn cells of the spinal cord by the anterior roots and motor fibres to the muscles. If the posterior roots of the lumbo-sacral plexus, or of the cervico-brachial plexus, be divided proximal to the ganglion, the apæsthetic limb is not used by the animal, there is a marked loss of tonus in the muscle, and a disuse-atrophy, though apparently no degeneration, occurs; the muscles can still be made to contract by stimulation of appropriate regions of the cortex cerebri, or of the nerves going to the muscles, as readily, if not more so, than on the uninjured side. If the anterior roots had been divided the muscles would have degenerated rapidly, and no such results from stimulation could have been obtained. The atrophic effects are still more marked if the anterior and posterior roots are *both* divided.

It is necessary to mention a few examples of *correlative atrophy* due to absence or recession of the normal physiological stimulus after amputation of limbs, especially when this has occurred *in utero.* Atrophy of the tracts and centres in the spinal cord and brain, which are concerned with the innervation of the part, may occur. Thus there is atrophy of the posterior column of the same side and of the antero-lateral of the opposite, and of that portion of the cortex cerebri which is normally concerned in voluntary movements of the limb. Atrophy of the frontal lobe of the left hemisphere has been found associated with atrophy of the opposite lateral lobe of the cerebellum. Atrophy of the fillet and the posterior column nuclei has resulted from porencephaly of the central convolutions of the cortex cerebri.

Atrophy of structures which undergo premature decay owing to *inherent* defect of the cell-elements adequately to nourish themselves.—Reference to the articles on "Primary Progressive Myopathic (Pseudo-hypertrophic) Paralysis," and on "Friedreich's Ataxia," will show that the only etiological factor which has been definitely shown to have a causal relation to atrophy of muscle and nervous elements in these diseases respectively is heredity. Facial hemiatrophy and sclerodermia from their distribution would suggest a trophoneurosis, although some authorities consider the condition as a primary wasting of the connective-tissue structures for which no reason is known. It is probable that inherent defect of the cells to nourish themselves is the determining cause of atrophy and degeneration. When the nutrient supply of the tissue is deficient in

quantity or altered in quality, these two factors co-exist, and may occasion a general atrophic or degenerative process in one or more of the master tissues of the body. When glandular, muscular, or nervous tissues begin to undergo nutritional change and decay, the effects become progressive and cumulative in proportion to the functional importance of the organ or tissue to the general nutrition of the body: for this reason we seldom find the morbid change in death from disease limited to one organ.

In all those chronic degenerative affections of tissues occasioned by such extrinsic causes as alcohol, accumulation of nitrogenous waste products in the blood, syphilis, and other toxic agencies (*e.g.* lead, etc.), the degenerative process may commence simultaneously in a number of different tissue-elements — glandular, muscular, nervous, and cardio-vascular: as we have less reason to believe that the above-mentioned extrinsic factors vary than the intrinsic, we must look to other causes for determining the seat in which the toxic agent will primarily produce the atrophy and decay. These causes may be found in the occupation and habits of the individual.[1] Given *stress* upon an organ or tissue, plus defective quality and quantity of nutrient supply, degeneration ensues. When, therefore, owing to changes in the blood and changes in the cardio-vascular system, waste is in excess of repair, atrophy and degeneration must occur.

Hereditary factors play a very important part in determining the primary seat of decay; and experience teaches that the more these factors enter into the equation of life, the more the value of x (the life of the individual) proportionately sinks; by no art of the physician can they be removed or modified. On the other hand, toxins can be counteracted by antitoxins, and injurious occupations and habits can be modified or abandoned. Rarely does one of these etiological factors act alone; as rarely are degeneration and atrophy found limited to a single organ or tissue, and the present discussion among pathologists whether atrophy of nervous, glandular, or muscular elements be primary or be secondary to the fibrous and vascular change, is of value in showing that the older pathologists were wrong in assuming that the associated fibrous and vascular changes are in all cases the primary cause of the atrophy; it is probably as erroneous to assume that the converse is invariably the order.

As inflammatory stasis, thrombosis, and embolism may cause necrosis, so may chronic degenerative changes in the cardio-vascular system be the primary factor in many instances of impaired nutrition and decay; although here again we are met by the argument that arteriosclerosis is itself a primary degenerative process, and the associated inflammatory changes secondary. Cirrhosis of the liver is usually cited as an example of a primary irritative hyperplasia of the fixed connective-tissue elements,

[1] Edinger first pointed out the importance of the occupation and habits of the individual in determining the primary seat of the degenerations of the nervous system, more especially in tabes and neuritis, and, moreover, endeavoured to prove it experimentally. In 1900 I (28) discussed the important relation of stimulus to degeneration, and in an article on Tabes in hospital and asylum practice I (29) brought forward instances in which stress of occupation apparently determined in a measure the seat of degeneration.

by the cicatrisation of which the epithelial cells are gradually strangled and undergo atrophy from default of nutrition. Even in the stage of enlargement, however, degenerative changes may have begun in the liver cells, and this is likely enough, seeing that they are only separated by delicate capillary walls from the blood containing the toxic agent. It must, however, be conceded that the liver cells depend upon the portal blood (which contains the toxic agent) for their functional activity, and upon the blood of the hepatic artery for nutrition. The liver is accordingly a debatable ground of these rival views. I am in favour of the view that the greater proportion of atrophic degenerative processes are due to primary retrogressive nutritional changes of the specialised cell-elements. The more highly specialised in function an organ or a tissue the larger the supply of nutriment, and the more likely are tissues of great physiological activity to undergo degeneration. The cell-elements of special function, when destroyed, are unable to regenerate, and repair by fibrous tissue takes place. This is particularly well shown in the central nervous system.

Nutritional Changes in Tissues highly specialised in Structure and Function.—The study of the development and of secondary degeneration of the nervous system shows the genetic and trophic independence of the nervous units; and in spite of the opposition which the "neuron theory" has lately met with, it is still acceptable to pathologists and neurologists, as it serves to explain the primary atrophic and degenerative processes of the nervous system.

The Structure of the Nerve-cell as revealed by the Nissl and Cajal Silver Methods.—The Nissl method is generally used for demonstrating the internal structure of the protoplasm of the nerve-cell and its processes, and is especially valuable in the study of pathological conditions. This method shows pictures of the nerve-cells stained in a characteristic manner. Examination of a typical structure, such as an anterior horn cell, stained by this method shows the following characteristics. The body of the cell appears a deep blue, but not uniformly, for the staining presents a mosaic appearance, due to lightly stained polygonal areas, disposed more or less concentrically round the nucleus and separated one from another by an unstainable substance. Towards the periphery of the cell these polygonal stained areas become elongated; upon the dendrons they are fusiform, their long axes being parallel to the processes. At one portion of the cell, if it is entire, a process—the axon—will be observed which does not possess any stainable substance, so that this method differentiates two substances—a chromatic stainable substance and an achromatic substance. (*Vide* Plate V. Fig. 1.) The stainable material is a nucleo-proteid, a substance which contains phosphorus, but in less proportion than the nucleic acid of the nucleus. The fact that the stainable substance is found around the nucleus may indicate that it is a result of the active metabolism exerted by the nucleus on the surrounding protoplasm. By some authorities it is considered to be a store of nutriment, by others a store of energy; and on this account it has

been termed by Marinesco "kinetoplasm." The changes that this substance undergoes, as studied by the Nissl method, show that it has some important functional relationship to the metabolic activity of the neuron; it is, however, not the essential substance. The unstainable substance, on the other hand, is essential, and consists of an organised network of delicate fibrils which extend into the dendrons, forming a network in the cell-substance and passing out again in the axis-cylinder process. Consequently there is a direct protoplasmic fibrillary continuity between the dendrons and the axon. (*Vide* Plate VI. Fig. 1.) The nucleus is apparently of simple structure and is permeated by irregular strands of karyoplasm which form a coarse network; it is apparently situated in the centre of the cell and contains a nucleolus or several nuclear bodies which, together with the nuclear membrane, stain with a basic dye. The large motor cells of the cord and brain are the best for studying nutritional changes in the cell-protoplasm, because the stainable substance in these structures appears normally as if it consisted of formed elements (Nissl granules) in the body of the cell and in the dendrons. I have always looked upon these elements as being due to a death-change of the fluid plasm of the cell whereby the nucleo-proteid substance contained in it is thrown down as a fine precipitate, much in the same way as myosin is precipitated from myosinogen. If this substance is abundant in the fluid plasm it produces when precipitated these definite forms, because it fills up the spaces of the unstainable intracellular fibrillary reticulum.

"Chromatolysis" is the term frequently applied to designate the disappearance or disintegration of these Nissl granules, and may present various stages. Usually the process begins at the periphery of the cell and in the dendrons. The stainable substance may be greatly diminished or entirely lost in these situations, or, again, the granules may be seen to consist of fine particles, their definite outline being lost, and in advanced chromatolysis the whole cell may be so affected. (*Vide* Plates V. and VI.) The condition and amount of the stainable substance may be looked upon as an indication of the nutritional condition of the cell and the potential of the neuron; and it is conceivable that diminution of the nucleo-proteid colourable substance is an expression of the diminution of the vital nutritional interaction of the highly phosphorised nucleus upon the surrounding cell-protoplasm. (*Vide* Plate V.) I consider that chromatolytic changes alone are not indicative of cell-destruction and neuron-degeneration; for marked chromatolytic changes may occur in the cells of origin after section of a nerve and yet the cells may completely recover; also after ligation of vessels causing only a temporary failure of blood-supply, similar marked changes may occur and yet the neurons may completely regain their form, structure, and function. (*Vide* Plate VI. Figs. 2 and 3.)

Changes of the cell in form and size may be recognised, *e.g.* swelling or shrinking, due no doubt to an alteration of the vital osmotic reaction of the cell-protoplasm to its fluid environment; likewise the nucleus may

be clear and swollen or shrunken, the nuclear membrane in the latter case being thrown into folds. Very frequently the nucleus becomes eccentric in position instead of being situated in the centre of the cell, and owing to abnormal osmotic relations and protoplasmic change it may even be extruded, and this of necessity would cause death of the cell. (*Vide* Plate VI. Figs. 2 and 3.) Another indication of death of the cell-protoplasm is revealed by uniform staining of the whole cell and its processes. It occurs in hyperpyrexia and in the coagulation-necrosis resulting from obstruction of the blood-supply for a sufficient length of time to cause the death of the protoplasm. (*Vide* Plate V. Figs. 2 and 3.)

Wallerian Degeneration.—Numerous observers have claimed that the law, formulated by Waller, to the effect that every part of a nerve which is separated from its cell of origin undergoes degeneration, whilst the rest remains normal, although fundamentally true, may require some modification; the first observer to suggest this was Dr. W. H. Dickinson, who, in a very interesting paper on "The Changes in the Nervous System which follow the Amputation of Limbs," stated as the result of his observations that the posterior roots may atrophy, though still in connexion with the ganglia, and the anterior though still in connexion with the cord; and it appears that long disuse of a nerve is sufficient to lead to its atrophy, although those nervous structures which immediately regulate its nutrition are complete.

The degenerations described by Waller and Türck are degenerations secondary to injury (*vide* Plate VI. Figs. 4, 5, 6, 7), and that described by Dr. Dickinson and numerous other observers since may be looked upon as a disuse-atrophy. A little later Gudden commenced his celebrated work upon atrophy of the cells of origin of a nucleus by tearing out the nerve in young animals, and by this method threw great light upon the anatomy of the nervous system. It was adopted with striking success by Forel and von Monakow.

There is another form of degeneration which, accepting the cellular theory of Virchow—that the whole organism, including the nervous system, is made up of an aggregation of cells, each cell being a living unit with an independent existence—is a primary degeneration of the complex nerve-cell or neuron. Each cell of the body nourishes itself and is not nourished—that is to say, every cell behaves as a unicellular organism possessing a specific energy; and by the vital reaction of its protoplasm upon the lymph environment metabolic exchanges, constructive and destructive, are continually taking place correlative with functional activity. We have no evidence to show that regeneration of nerve-cells can take place in the higher vertebrates, but there is evidence in favour of the view that all the nerve-cells of the adult body are present in a rudimentary form at birth. The growth of the nervous system depends not so much upon an increase in number of the nervous units, but in their extension by multiplication and complexity of the processes.

Two Forms of Nervous Degeneration.—There are two forms of degeneration: (i.) Secondary (Wallerian) degeneration, due to the interruption of the axon when it is cut off from its cell of origin, as, for example, section of a nerve or a focal transverse lesion of the spinal cord produced by disease or injury. Systems of fibres which have their cells of origin above the lesion degenerate downwards, and may be recognised, when the tissues are stained by the Marchi method, by the black stained products of degeneration occupying different areas corresponding to definite systems of efferent neurons, whilst tracts of fibres conducting afferent impulses having their cells of origin in the spinal cord or posterior spinal ganglia below the lesions have a normal appearance. The converse applies to tracts above the lesion. Therefore *secondary* degenerations, whether occurring as the result of experiment or disease, generally arise from conditions outside of the neuron; for, of course, a hæmorrhage or vascular occlusion followed by local softening may either destroy the groups of ganglion cells from which the fibres arise, or interrupt the fibres; in the former case the neuron will die as a whole; in the latter, only the portion which is cut off from the cell of origin, which is, of course, the trophic centre of the complex branching protoplasmic unit—the neuron.

(ii.) Primary degenerations are clinically and pathologically different from secondary. They are evidences of nutritional failure of the neuron from inherent or acquired defect of durability. They arise as a result of altered conditions of the blood and lymph, due generally to the introduction or generation within the body of poisonous substances, and are insidious in form, progressive in character, and generally fatal in termination. They are influenced by hereditary or acquired tendency to nervous degeneration, and the election of the particular system or systems of neurons causes definite groups of clinical phenomena which admit of empirical classification into definite diseases. They may affect primarily one or more of three sets of neurons. (1) *Afferent*, of which the best example is tabes dorsalis; (2) *Efferent*, of which the best examples are idiopathic lateral sclerosis, amyotrophic lateral sclerosis, and progressive muscular atrophy; (3) Associational, of which a good example is progressive dementia in the early stages. The afferent and efferent systems may be simultaneously affected in hereditary ataxy, and in progressive paralytic dementia the higher cortical association systems degenerate first, but sooner or later the progressive paresis and physical signs indicate that the efferent system is also degenerating. Again, in the tabetic form of this disease the afferent system of neurons is affected with the associational. The accompanying figure (Fig. 39) illustrates these three sets of neuronic systems, and it shows why the most remote parts of the neurons, viz. collaterals and the terminal arborisation of the axon the farthest removed from the trophic centre of the cells of origin, should in these primary degenerations be the first to smoulder away in the process of degeneration.

Atrophy of the cell-elements of glands, as of the *kidney*, may be due to defective blood-supply consequent on change in the arterial walls;

the very conditions which are said to give rise to changes in the arterial walls may likewise cause degenerative change of the epithelial elements: yet in those cases in which the kidney is not much shrunken, but in which the arterial changes are great, the primary degeneration is probably in the arteries, *e.g.* syphilitic renal disease. In the granular contracted kidney the opinion that the primary change is a fibrosis, causing atrophy of the epithelium of the uriniferous tubules, is being given up in favour of the inference that a retrograde nutritive change with secondary fibrosis occurs.

Atrophic Changes of Muscle.—In the *heart* fibrous tissue is frequently found replacing muscular tissue; and this condition is termed *fibroid heart*, as if the fibrous-tissue overgrowth were the morbid change that produced the atrophy of the muscular fibres. On the contrary, most of such cases are primary degenerative atrophy of the muscular fibre owing to impaired nutrition. When a branch of the coronary artery is blocked by thrombosis or embolism, coagulation-necrosis of muscular fibres takes place, and myomalacia results. Although insufficient for the specialised elements, the nutrient supply of the fibrous tissue is unaffected; it receives in fact excess of nutriment, and undergoes a compensatory hyperplasia, which really amounts to a process of repair, and should be considered as a healing process as much as the fibrous-tissue formation which unites the two parts of a severed muscle. Perhaps the best example of primary atrophy of muscle with secondary fibrous overgrowth of connective tissue and fat is afforded by Duchenne's paralysis, in which pseudo-hypertrophy occurs. Erb's paralysis is the same disease in the atrophic form; in it there is no overgrowth of fibrous tissue, but atrophy of the muscle only,—a clear proof that the muscular atrophy in the former is not consecutive to the fibrous overgrowth.

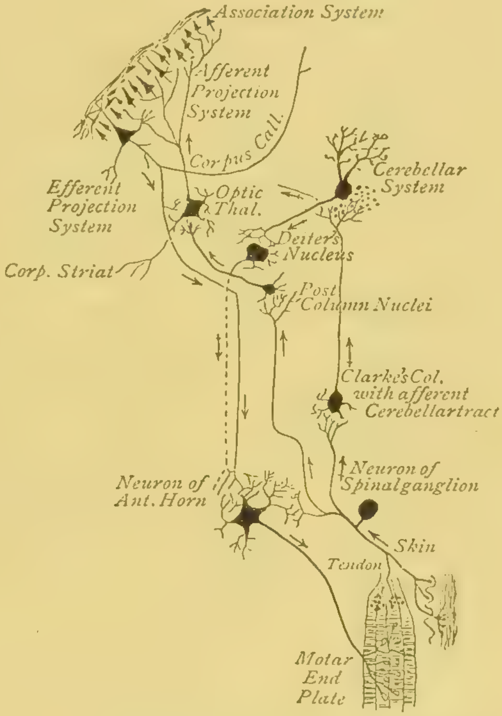


FIG. 39.—Diagram illustrating the afferent, efferent, and association systems of neurons. It will be observed that there are three nervous circles. In voluntary movements impulses are travelling along all these systems. In tabes there is degeneration and interruption of the afferent path in spinal, cerebellar, and cerebral systems; consequently inco-ordination of voluntary movements. Diagrammatically the posterior spinal ganglion is represented as giving off three processes; more probably it only gives off one.

Looking upon tissues as composed of living protoplasmic units specialised and non-specialised in function—the former endowed with high metabolic activities, the latter with low—nearly all the nutriment

which goes to healthy gland, muscle, or nervous matter is utilised by the special cell-elements. Where fibrous connective tissue exists alone the blood-supply is extremely small and the metabolic exchange trifling; consequently the connective tissue of an organ with a large vascular supply would, by receiving excess of nutriment, undergo hyperplasia (*vide* "Hypertrophy") if the specialised element were unable to utilise that nutriment. Thus coexistent with atrophy of one there is hypertrophy of the other; the latter resulting from the former, and not the converse. For the microscopical changes observed in these organs and tissues the reader is referred to the special articles. Pulmonary emphysema may be mentioned as an example of atrophy of blood-vessels and interalveolar connective tissue (particularly the elastic); but this is always associated with changes in the epithelium, and generally with degenerative conditions in other organs.

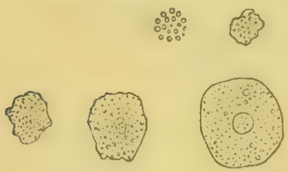


FIG. 40.—Atrophied liver cells from cyanotic atrophy of the liver in different stages of degeneration (× 400 diameters).—*Hamilton.*

Mechanical engorgement is by some authors regarded as a cause of atrophy of the specialised cell-elements by undue *pressure*, *e.g.* cyanotic atrophy of the liver in prolonged mitral disease.

THE ALBUMINOID DEGENERATIONS.—Certain closely related chemical substances, the result of proteid metamorphosis, are the cause of amyloid, hyaline, mucoid, and colloid degeneration in certain tissues of the body.

Amyloid or Lardaceous Change is far less commonly met with now than before the era of aseptic surgery. The causes are generally prolonged suppuration and ulceration; thus it is met with in caries and necrosis of bone, chronic empyema, pyonephrosis, tuberculosis, especially of the lungs and osseous system, syphilitic disease, actinomycosis, and chronic dysentery. It also occurs in syphilis and in rare instances in cachectic diseases without suppuration, *e.g.* malaria, cancer, and leukæmia. Lardaceous disease therefore does not constitute a clinical entity, and indeed may produce no defined clinical symptoms excepting albuminuria and diarrhœa.

Morbid Anatomy.—Amyloid change specially affects certain organs, which are in order of frequency the spleen, kidney, liver, the large blood-vessels, the mucous membrane of the intestines, the lymphatic glands, the osseous system, the suprarenal bodies, and the heart. It rarely affects the lungs, the bladder, and genitals, very rarely, if ever, the voluntary muscles and the integument, and never the central nervous system. The amyloid bodies found in the latter and in the prostate are discussed elsewhere. The organs affected are enlarged and their specific gravity increased. The tissue cuts firmly and leaves a sharp edge, and when the change is advanced resembles bacon rind, and has a glistening, waxy, translucent appearance which, however, is not always uniformly distributed through the organ: thus in the spleen the Malpighian bodies may be especially affected, hence the term "sago spleen," from their

resemblance to grains of boiled sago. A moderate degree of change may not present any macroscopic appearances; in fact, apparently quite normal tissues, or tissues which are the seat of engorgement or associated fatty degeneration, may only reveal evidence of the amyloid disease by appropriate chemical reactions and microscopic examination. An organ in which this change is suspected should be treated as follows: A little Lugol's solution (iodine dissolved in water containing a little iodide of potassium) should be poured over the cut surface, when a mahogany red colour will be produced by the amyloid material; by treating with sulphuric acid or chloride of zinc this colour is changed to blue.

Microscopic Appearances.—In sections treated with methyl aniline violet, or gentian violet, the amyloid substance is stained rosy pink instead of blue, which is the colour the normal tissues are stained. Microscopic examination shows that the change affects especially the intima and media of the blood-vessels, the adventitia being rarely affected and the endothelium apparently never. The fixed connective tissues of the organs are affected, while the glandular and lining epithelium is never involved. The appearances are very characteristic in the Malpighian corpuscles of the spleen and the glomeruli of the kidney. The amyloid material may appear as streaks or clumps in the interstitial tissues of the parenchyma, and may cause, or be associated with, degenerative or atrophic changes of the cells. When unstained the affected tissue shows streaks and islands of glistening homogeneous substance. The substance resists bacterial decomposition and the action of the gastric juice.

Pathology.—Since amyloid substance is not universally deposited, it cannot be solely caused by a blood change; it would rather appear to be the result of an interaction of nutritionally altered cells of certain organs and tissues with the chemically altered lymph by which they are surrounded. Amyloid material is said to be a combination of chondroitin-sulphuric or chondroitinic acid [$C_{18}H_{27}NSO_{17} + H_2O = H_2SO_4 + C_{18}H_{27}NO_{14}$ (chondroitin)] with a proteid; but chondroitinic acid is normally present in bone, cartilage, and elastic tissue; it is therefore possible that this pathological substance is the result of an abnormal combination of normal substances. It is said that aseptic suppuration set up by turpentine injection can produce this change although the conditions of disease in which it is ordinarily met with suggests that bacterial influences are all-important in its production.

Mucoid Degeneration.—Mucoid degeneration may affect connective tissues, cartilages, bones, and all the tissue-elements of tumours; it is generally accompanied by softening and often by the formation of cysts. It must be distinguished from hypersecretion of mucin as a result of inflammation or irritation of mucous membranes. It is a metamorphosis of protoplasm into mucin in an abnormal situation, viz. in mesoblastic tissues. Widespread mucinoid degeneration of the subcutaneous tissues has been described in myxœdema, and has been explained by supposing that an altered condition of the blood-plasma, due to thyroid defect, leads to an abnormal bio-chemical reaction of those tissues on their

fluid plasma environment. The name myxœdema was originally given to the disease on the supposition that excess of mucin in the subcutaneous tissues explained the swelling. The term is, however, a misnomer. There is certainly an overgrowth of connective tissue, mainly fat; but in the earlier stages of the disease, before the new connective tissue has become converted into fully formed areolar and adipose tissue, there is, as in all new connective tissues, a relatively large proportion of ground substance or matrix, and so an increased proportion of the principal constituent (mucin) of the matrix (Halliburton). Death of the cells in rapidly growing neoplasms may be the result of mucoid degeneration of the protoplasm, and this transformation may be met with in various benign and malignant growths, such as lipomas, chondromas, and sarcomas and carcinomas, and especially in the myxomas, in which mucin is the essential element. When tumours undergo this degeneration cysts are usually formed along with the mucoid infiltration. Ovarian tumours are especially liable to undergo this form of cystic degeneration. Mucin is a glyco-proteid devoid of phosphorus; its carbohydrate constituent (glucosamine) has the power of reducing cupric sulphate in alkaline solutions. There are many varieties of mucins, physiological secretions of different varieties of epithelium, and still more varieties of pathological mucins.

Hyaline Degeneration.—This regressive metamorphosis consists in the formation of a homogeneous proteid substance of an obscure nature, closely related to the products of the other forms of proteid metamorphosis, into which it may pass. It is also related to coagulation-necrosis. It cannot be detected by the naked eye, but microscopically this change may be found in three chief sites. (i.) In the blood-vessels in old age, arteriocapillary fibrosis, arteritis, especially of the central nervous system, causing thickening of the walls and narrowing of the lumen. Perivascular hyaline change is present in tumours, especially peritheliomas (cylindromas); (ii.) It occurs also in all those conditions of organs and tissues which are associated with coagulation-necrosis and fibrinogenous exudations; (iii.) It may also occur in the interstitial tissues, but whether it is formed there or deposited there has not been decided. Its chemical characters are not satisfactorily determined. According to von Recklinghausen it is an albuminoid product which possesses reactions very analogous to the other products of proteid metamorphosis. Round bodies having a hyaline appearance and staining with acid fuchsin are found within and between the cells of epithelial cancers; these are known as Russell's fuchsin bodies (*vide* p. 611). As they resemble and react to dyes like hyaline substance, it is probable they have a similar chemical composition.

Colloid Degeneration.—The thyroid and pituitary glands normally secrete a colloid substance. This form of degeneration is especially liable to occur in those organs where colloid is normally formed, and it is met with therefore in goitre and tumours of the thyroid gland and hypophysis cerebri. Colloid degeneration in new growths apart from these situations is rare. The areas undergoing colloid degeneration may form large cystic

collections with thin walls; close by, there may be smaller microscopic areas, or areas just visible to the naked eye, of a substance looking like glue. The cysts are no doubt formed by the coalescence of these colloidal areas, and owing to serous transudation occasioned by vascular disturbances the colloidal substance is dissolved, and thus the cysts are often seen to consist of a number of thin-walled compartments containing a dark chocolate-coloured fluid.

FATTY METAMORPHOSIS.—Fatty degeneration is one of the most frequent and most important of the pathological conditions associated with lowering of function and destruction of cell-protoplasm. It is of especial interest to the physician, as it often affects vital organs and tissues, and is the cause of death in many diseases and in certain forms of poisoning. The existence of fat in the tissues may be studied by two different methods: (1) The macroscopic or microscopic visual demonstration of fat within tissues; (2) The extraction of the fat from tissues by ether in appropriate apparatus, an estimation of the quantities obtained, and a determination by chemical analysis of the nature of the extracted substances.

The macroscopic evidence of fat in tissues and organs may be obvious by the changes in the physical characters, *e.g.* the yellow or buff colour, greasy feel, indistinctness of the normal appearances, and, in the case of some organs and tissues, such as the liver and heart, by the increased friability. Teased preparations or frozen sections mounted in water or glycerin may reveal highly refractile droplets which disappear with ether, but a more complete study of fat within the cells or fibres can only be obtained by examining stained teased preparations or sections. The method generally adopted is to fix the tissues in osmic acid or Marchi's fluid (1 part 1 per cent osmic acid and 2 parts Müller's fluid). The advantage of this method is that it *fixes* the fat particles and stains them black, so that sections can be cut in paraffin or celloidin and mounted in the ordinary manner. The disadvantage is that only olein or the acid radical oleic acid is stained by osmium tetroxide; consequently negative results by this method do not prove the absence of fat, for stearin or palmitin or their acid radicals would not be stained. Schaclach R has the advantage of staining all forms of fat; it does not fix it; the sections, therefore, are prepared by the freezing microtomes, and after staining must be mounted in glycerin. Christian maintains that errors have arisen from reliance on the osmic acid method.

Fatty Infiltration, *vide* article "Obesity."

Fatty Metamorphosis of the Cell-Protoplasm may be a physiological process—as when the uterus undergoes involution after parturition; or the cells of the ruptured Graafian follicle undergo fatty degeneration, forming the corpus luteum; or the central cells of the acini of the mammary glands form colostrum corpuscles. The above-mentioned instances of fatty degeneration show that rapidly proliferating cells will undergo retrogressive nutritional change unless supplied with a proportionate

supply of nutriment. The uterus undergoes this retrogressive metamorphosis because the fœtus—the physiological stimulus which determines the increased flow of blood to the organ—has been expelled. The central cells of the mammary acinus undergo fatty degeneration because the peripheral cells require and take all the nutriment. For the same reason, probably, fatty degeneration occurs in the centre of new growths, especially when they are of rapid formation.

It is probable that the cells, thus deprived of adequate nutriment, behave like the starving animal, and liberate vital energy by using up their own protoplasm. In the starving animal, however, there is no deposition of fat granules in the cell, but atrophy only. If, however, a poison, such as phosphorus or CO, be administered to starving animals, then the urea eliminated is increased and fat is formed. Both these poisons interfere, as we shall see, with oxidation processes; the former by a process not satisfactorily explained, the latter by turning out the oxygen from its combination with hæmoglobin. The fat which accumulates in muscle-fibres undergoing fatty degeneration is formed for the most part out of organ-proteid by the splitting up of the latter into an amido-product which will be oxidised into urea, fat remaining behind if there be insufficient oxygen for its combustion. Another source of fat may be the decomposition of lecithin; concerning this source, however, there is a difference of opinion. Many physiologists, including Pflüger, deny that body-fat is formed from ingested proteid, and believe that it is formed from carbohydrates and fat taken in the food; moreover, it is considered that the fat of milk is derived from the body-fat, and that there is no evidence of Virchow's view that fat is formed from proteid.

Experimental Pathology of Fatty Degeneration.—Voit and Bauer showed that animals which had been starved, and were eliminating a constant of N in the form of urea, after the administration of small doses of phosphorus suddenly eliminated a great increase of N; while at the same time the oxygen taken in and the CO_2 given out were considerably diminished. These facts are clearly associated with the macroscopic, microscopic, and chemically demonstrable fatty degeneration of the striped muscles, the heart, the liver, and kidneys. In 100 parts of the dry substance the ether extract is

	Healthy Dog.	Dog poisoned by Phosphorus.
Muscle . .	16·7 per cent	42·4 per cent
Heart . .	9·2 ,,	20·4 ,,
Liver . .	10·4 ,,	30·0 ,,

It might be said that the diminution of O intake and CO_2 output was due to blood destruction, but the experimenters were unable to find evidence of this.

According to Gaule, some of the fat may arise from the formation of lecithin. He maintains that the primary change in phosphorus poisoning is in the nucleus. According to Krehl, only a very inconsiderable portion of the fat in fatty degeneration of the heart arises from this

source, and the lecithin is not appreciably increased. Slow poisoning by carbon monoxide produces fatty degeneration. This gas turns out the oxygen, forming a more stable compound with hæmoglobin than does oxygen, and produces the same effect on the tissues as profound anæmia, viz. deprivation of oxygen. But prolonged insufficiency of oxygen means also a lowered vitality of the cell-elements ; and it may be that the cause of the fatty metamorphosis of the cell-protoplasm in this form of poisoning as well as in phosphorus poisoning can be thus explained. The fact that CO, administered to starving dogs, increases the urea output, shows that there is an increase in destruction of organ-proteid and deposition of fat owing to insufficiency of oxygen. The object of using starved animals is, of course, to prove that the increased N must come from tissue-metamorphosis. But in phosphorus poisoning the same result is not explained by alteration of the blood ; and in my opinion too little stress has been laid upon tissue-respiration. We have seen that the cells nourish themselves and, probably by virtue of nucleo-albumins combined with ferric oxide, have the power of taking up oxygen and storing it in the protoplasm. It is probable that phosphorus damages the cells and interferes with this oxygen storage by the tissues ; hence less oxygen could be taken up by the blood, less CO_2 given off, and no appreciable change in the hæmoglobin value would be evident. Starving animals from whom large quantities of blood have been abstracted pass an increased amount of urea.[1]

Litten showed that rabbits and guinea-pigs, which had been kept three to six days in an atmosphere of 36° C., showed fatty degeneration of the heart, striped muscles, liver, and kidneys. This would seem to indicate that a high temperature maintained continuously in animals which have a relatively low capacity of heat dissipation (thermolysis) produces fatty degeneration, and supports the view that fever may produce fatty degeneration. Experiments upon such animals as rabbits are not always to be accepted as conclusive ; and Naunyn has shown that such animals may be kept thirteen days at a temperature of 36° to 40° without any fatty metamorphosis, provided they receive abundance of green food and the warm chamber be properly ventilated. In fever there is certainly increased organ-proteid destruction ; but according to Krehl, there is no parallelism in man between the height of the fever and the fatty degeneration of the muscles. Much would depend upon the effect of the toxins upon the muscles, the nerves, and their endings in the muscles.

Recent observations by careful experimental, chemical, and microscopic methods have thrown doubts upon these results of phosphorus poisoning and fatty metamorphosis, and it is necessary to relate briefly the experiments of Lebedeff, Rosenfeld, and others who have

[1] Araki, working in Hoppe Seyler's laboratory, showed that one effect of lessened oxygen supply was the presence of lactic acid in the urine, sometimes of sugar and albumin. Poisoning by CO, curare, and strychnine gave corresponding results, as also after epileptic seizures when the respiration was retarded. Diminution of oxidation processes is a factor common to all these conditions, and doubtless a primary cause of the abnormal metabolism.

studied the question with the view of disproving the generally accepted doctrine of Virchow that the cell-proteid was the source of the fat in fatty metamorphosis. Their experiments tend to show that the fat found in degenerated tissues was transported from the various normal fat depôts of the body and did not arise within the damaged cells from the incomplete oxidation of cell-proteid. Rosenfeld starved dogs until their fat was reduced to a minimum; he then fed them on lean meat and mutton fat until their fat depôts were stored with mutton fat, which has characteristic chemical qualities. These dogs with their store of mutton fat were then starved until there was no fat in the liver, although their fat depôts still contained mutton fat. Phosphorus was then administered, which brought about the appearance of fat in the liver. Chemical analysis of the fat extracted from the liver showed that it had the characters of mutton fat and not of the fat normal to dogs; the inference is that it had been transported from the fat depôts where it had been stored and did not arise from the cell-proteid. In confirmation of this it was found that starved dogs in which all the fat had been used up, when poisoned with phosphorus, showed no fatty degeneration, because there was no fat to transport. It is claimed also that there is considerable morphological evidence of fat transportation, and that there is no fat deposited when there is no circulation; further, it is only damaged cells, not dead cells, which can take up fat. Even Christian, in an admirable summary on "Some Newer Aspects of the Pathology of Fat and Fatty Degeneration," while strongly advocating this view, admits that Rosenfeld's own careful analysis of normal and abnormal kidneys—in which he shows that whereas in the former extraction by ether does not yield more fat in the degenerated organ than in the healthy, although visibly demonstrable in the former and not in the latter—is against the assumption that all the fat in fatty degeneration is transported to the cell. Moreover, tissues removed aseptically and preserved, according to many observers, show fat droplets (autolysis).

Diseases in which Fatty Degeneration occurs.—In the different grave forms of *anæmia*, particularly *pernicious anæmia* and *hæmorrhagic purpura*, fatty degeneration of the muscular substance of the heart occurs, whereas other muscles in the body are not affected. It may occur after severe hæmorrhage. We may then ask, Why should the *heart* undergo this degeneration and other muscles escape? Several factors seem to be at work in producing the metamorphosis of the cell-protoplasm. In chlorotic anæmia the hæmoglobin value of the blood may fall as low as in pernicious anæmia; yet in the former fatty metamorphosis seldom, if ever, occurs, whereas in fatal cases of the latter it is never absent. Other factors then are present besides deficiency of oxygen. In both diseases the work done by the heart is increased. In pernicious anæmia there must be other causes, possibly one or more of the following: the diminution of the quantity of blood; the alteration in the quality as shown by the great diminution of the specific gravity; the great deficiency of iron in the pigment of the blood, and consequent diminution of the

oxygen-carrying value; and the presence of toxins in the blood. That many of these factors act together in producing the metamorphosis of the cell-protoplasm is clear, and that the heart muscle is selected, and the voluntary muscles spared, prove that not the least important factor is work with inadequate repair of waste; for while, on the one hand, the feeling of languor and indisposition to work, which is a prominent symptom of anæmia, imposes rest upon the voluntary muscles, and therefore a lowered metabolism in conformity with the depressed vital activities of these tissues, the heart on the other hand must, by its automatic activity, do even more work in order to supply the necessary oxygen and nutrition for the nervous system. The diaphragm may be similarly affected; for on account of the "air-hunger" it must do proportionally more work than other striped muscles. There are, moreover, certain other facts in pernicious anæmia which support the hypothesis of the origin of fat by the disintegration of organ-proteid, viz. the abundance of subcutaneous fat and the large amount of N eliminated by the urine—generally more than can be accounted for by the food. Some years ago I examined the heart, skeletal muscles, and kidneys of a large number of general paralytics and epileptics dying after prolonged convulsive seizures or status epilepticus, by the osmic acid method only; all these cases showed evidence of fatty changes in the muscular fibres, in a measure proportional to the length of time and severity of the convulsive seizures and the venosity of the blood and asphyxial conditions. Rightly or wrongly, I attributed the existence of the fat in the tissues to deficiency of oxygen owing to the prolonged and increasing venosity of the blood and the excess of katabolic over anabolic processes in the muscles excited to continuous tonic and clonic spasms. In confirmation of this view it may be stated that general paralytics and epileptics dying without antecedent convulsive seizures did not show this reaction in the muscles. There are indications also that the blood in these conditions may contain fat particles, and I attributed the fat in the cells of the kidney and liver rather to transportation than to degeneration.

Another frequent cause of fatty degeneration of the heart is *partial occlusion* of the *coronary arteries* by atheroma. A large proportion of the cases of fatty degeneration of the heart in people who have passed middle age are of this origin. Sometimes one or both coronary arteries may be obstructed with or without valvular disease, and the occlusion may be so great that the artery may admit a bristle with difficulty. As one coronary artery, or a branch of one, may be obstructed, the fatty degeneration may be local, affecting only one side of the heart—more often the left which has the most work to do; but the auricles are usually not affected in such cases.

Certain toxic agencies, besides phosphorus and carbon monoxide, produce fatty degeneration, viz. arsenic, antimony, sulphuric acid, nitric acid, chronic alcoholism, and, lastly and most important, *toxins*—the products of microbic infection and growth.

Finally, fatty degeneration may be the expression of the gradual running down of the vital mechanism: we have supposed that every particle of living protoplasm is endowed with a certain amount of endurance, and when the limit of the life of the cell is approached, fatty degeneration occurs: in this way we can explain the *senile fatty metamorphosis* of cartilage cells and the excess of fuscous pigmentation of the ganglion-cells of the central nervous system; most of such pigment being really of a fatty nature. We thus see that fatty degeneration is the result of a lowered vital activity of the cell or fibre, and the conditions which give rise to it are complex, but depend essentially upon—(1) Failure of nutrition of the cell, which makes it unable to repair and compensate for the waste; (2) Breaking down of the cell-protoplasm and formation of amido-antecedents of urea and of fat out of organ-proteid; (3) Insufficiency of oxygen-supply by the blood, or incapability of the cell itself to take up sufficient oxygen to oxidise the fat, hence accumulation of a deposit within the cell or fibre; (4) Damage or injury of the cells and transportation of fat from the normal fat depôts. At present the extra-cellular origin of fat in fatty degeneration of organs is probably conclusive in respect to the liver, but not as regards muscle and kidney.

The Chemical Composition of Nervous Tissue.[1]—The nervous system consists of water and various complex solid organic substances and inorganic salts. The amount of water varies; it is most abundant in the grey matter, or in those regions of the nervous system where the proportion of grey matter is greatest. No doubt this is partly due to the much greater vascularity of the grey matter. Thus the sciatic nerves contain 65·3 per cent of water, the white matter of the cerebrum 68 to 72 per cent, and the grey matter from 81 to 86 per cent. The solids of the nervous tissue are—(*a*) proteids, comprising in the grey matter 50 per cent of the solids; (*b*) nuclein from the nuclei of the cells; (*c*) neuro-keratin, the chemical substance found in the neuroglia; (*d*) phosphorised fats, protagon and lecithin; (*e*) cerebrins or cerebrosides; (*f*) cholesterin; (*g*) extractives; (*h*) gelatin; (*i*) inorganic salts, especially alkaline phosphates and chlorides.

The Proteids.—There are three kinds of proteid, differing in the temperature at which they are coagulated by heat, in the readiness by which they are precipitated by acetic acid and by neutral salts; one of them contains 0·5 per cent of phosphorus and is a nucleo-proteid differing from the other two. This nucleo-proteid is the substance of the nerve-cells stainable by the Nissl method, and no doubt plays a very important part in the metabolism of the neuron.

The Phosphorised Fats.—Lecithin, kephalin, and the compound of lecithin with cerebrin, which is called protagon, belong to this group. The bulk of the organic phosphorus is contained in the lecithin, which may

[1] In the first edition of this work these earliest observations relating to the chemistry of degeneration of the nervous system were first published. Since then I have had the great advantage of collaborating with Professor Halliburton, and in a long series of observations based upon experimental, pathological, and clinical studies, have extended and confirmed the premises of these initial observations.

be taken as the type of phosphorised fats; it is an abundant constituent of nervous tissue, but there are several lecithins differing in the kind of fatty acid. The white matter of the cerebrospinal nervous system consists largely of lecithin, the chief constituent of myelin. When degeneration of nervous matter occurs the lecithin is hydrolysed and splits up thus:

$$\underset{\text{Lecithin.}}{C_{44}H_{90}NPO_9} + \underset{\text{Water.}}{3H_2O} = \underset{\text{Stearic acid.}}{2C_{18}H_{36}O_2} + \underset{\text{Glycero-phosphoric acid.}}{C3H_9PO_6} + \underset{\text{Cholin.}}{C_5H_{15}NO_2}$$

The fatty acid represented in the above equation is stearic acid; but oleic acid is also present. Now oleic acid is an example of an unsaturated fatty acid, and hence possesses an affinity for oxygen. It is well known that fat blackens osmic acid, because it takes oxygen from it and forms a lower oxide of a black colour. Fats which are saturated like the glyceride of stearic and palmitic acids do not give this reaction. The reason why nerve-fibres become black when treated with osmic acid is that the lecithin of the myelin contains oleic acid.

The nitrogenous derivative of lecithin, cholin, belongs to the trimethylamine series, of which neurin, muscarin, and betain are other examples.

$$\text{Cholin}\ \begin{array}{l} CH_2OH \\ | \\ CH_2 \\ | \\ C = N(CH_3)_3 \\ | \\ OH \end{array} \qquad \text{Neurin}\ \begin{array}{l} CH_2 \\ \| \\ CH \\ | \\ C = N(CH)_3 \\ | \\ OH \end{array} \qquad \text{Muscarin}\ \begin{array}{l} CH_2{<}^{OH}_{OH} \\ | \\ CH_2 \\ | \\ C = N(CH_3)_3 \\ | \\ OH \end{array}$$

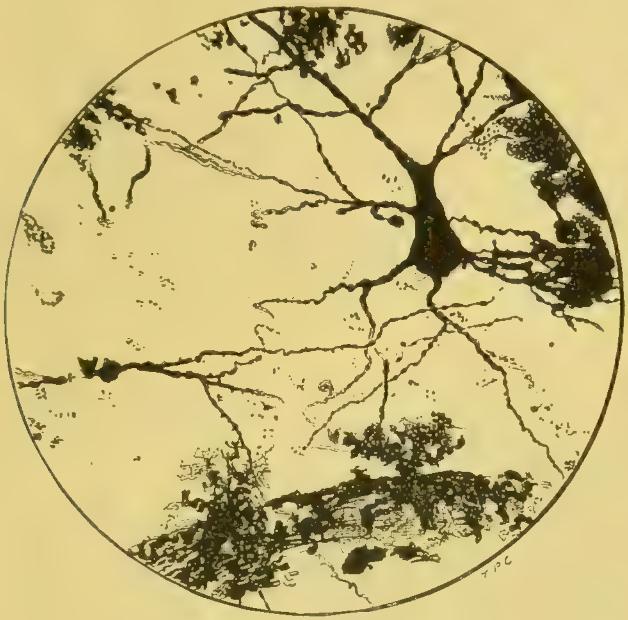
Cholin was at one time thought to be identical with neurin, and the two are very closely related, cholin being readily converted by bacterial agencies into neurin by the removal of two molecules of hydrogen and one of oxygen, a point of considerable importance, as neurin is one hundred times more poisonous than cholin.

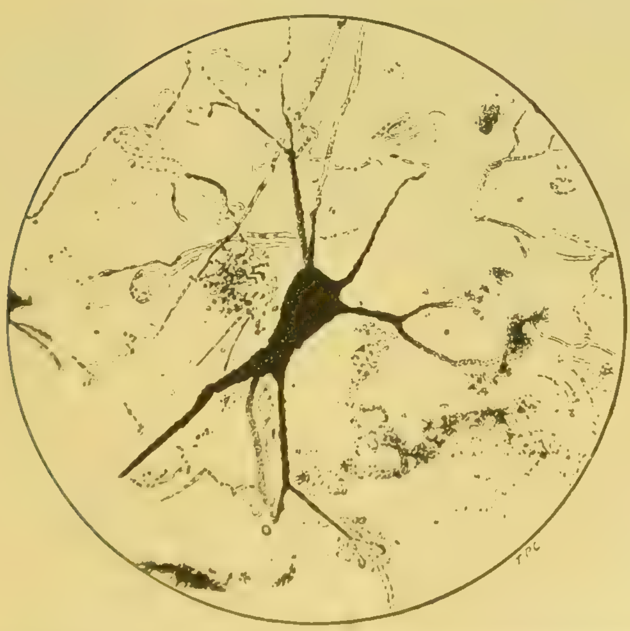
Fatty Acid Products.—When nervous tissue undergoes degeneration the products of the decomposition either remain in the tissues, to be removed by absorption and phagocytosis, or are carried away by the blood and cerebrospinal fluid. The fatty acids remain behind in the sheaths of the nerve-fibres and in leucocytes, and by virtue of the affinity of the oleic acid for oxygen, even after the tissue has been fixed in Müller's fluid, these particles of fatty acid of various forms and sizes stain black by the action of the osmic acid contained in the Marchi fluid (*vide* Plate VI. Figs. 4, 5, 6, 7); whereas normal nerve placed in Müller's fluid, and subsequently in Marchi fluid, is not so stained, since the lecithin has been fixed by the chromic salt. In degeneration of the peripheral nerves, caused by section of two or three months' standing, the fatty acid products of degeneration are *completely* removed, and about this time the

delicate myelinated new regenerated fibres make their appearance, and this is accompanied by the presence of organised phosphorus, which can be detected by analysis. In the central nervous system of the higher vertebrates, where regeneration does not occur, absorption of the fatty products of degeneration is much slower.

Cholin.—The existence of cholin may be recognised by (1) physiological and (2) micro-chemical tests. (1) A saline solution of cholin, of cholin hydrochloride, and of the residue obtained from the alcoholic extract of the cerebrospinal fluid and blood of (*a*) animals in which experimental lesions of the central or peripheral nervous system have produced active degeneration, or (*b*) from patients suffering from any form of disease involving active degeneration of the myelin, produces a similar physiological reaction. The reaction is—A temporary fall of blood pressure after intravenous injection in animals, which is partly cardiac and partly due to dilatation of peripheral blood-vessels. The alkaloid acts directly on the neuro-muscular mechanism of the blood-vessels themselves. Many substances produce this fall of blood pressure, but, with the exception of spermin, no other substance gives the peculiar result which follows the injection of a small dose of atropin. Thus, if a saline solution of the alcoholic extract of blood to be tested has already given a fall of blood pressure, and then a small dose of atropine be administered, the same solution no longer gives a fall but a rise of blood pressure, or, at any rate, the fall is abolished. The (2) *Micro-chemical tests* are—(A) by the formation of octahedral crystals of the platino-chloride of cholin, and (B) by the iodine test. The former test can be applied thus. The blood or cerebrospinal fluid is allowed to stand for twenty-four hours with about five times its volume of absolute alcohol. The alcoholic extract is filtered off and evaporated to *dryness* at a temperature not exceeding 40° C.; it is then taken up with *absolute alcohol* (*water-free*), filtered, and again evaporated to dryness at 40° C. This is repeated several times in order to remove the inorganic salts. The final residue is dissolved in 15 per cent alcohol and a slight excess of platinum chloride solution is added. Allow a few drops to crystallise on a slide, and on examination under the microscope yellow octahedral crystals of platino-chloride of cholin will be seen. (B) To a portion of the final residue dissolved in 15 per cent alcohol, add a few drops of a solution of iodine dissolved in potassium iodide; a brownish precipitate denotes the presence of cholin.

Toxins, the chemical products of certain pathogenetic micro-organisms, sometimes produce fatty degeneration of the muscles. Dr. Sidney Martin has found intense fatty degeneration of the muscles and segmental degeneration of the nerves to result from injection of the diphtheritic toxin. I have observed intense fatty degeneration of the heart in a case of diphtheritic paralysis, but I could find no degeneration of the nerve-trunks. It has seemed to me that toxins which produce degeneration act either upon the motor end-plate like curare, or upon the nerve-cell; but the effect of the poison is manifested in the former case by fatty change of the muscle, in the latter by degeneration of the outgrowth of





Figs. 41 and 42.—Photomicrographs of two pyramidal cells from a case of general paralysis of the insane, magnified 400 diameters. The specimen is stained by the Golgi quick method, and the two cells were found in the same section at no great distance from one another. Fig. 41 represents a large pyramidal cell with its branching *dendrons* in a fairly healthy condition; these are connected with [illegible] glia cells (or rather lymph-spaces surrounding cells), which are seated upon a perivascular lymphatic. According to Cajal, these cells may act as *local vaso-dilators* by contraction of their pseudopodia. From the middle of the base of the cell is seen a *neuron* giving off a *collateral*. Fig. 42 is a large pyramidal cell undergoing atrophic degeneration.

the nerve-cell (viz. the nerve-fibre), as well as of the muscle. Acute atrophy of the liver is probably due to microbic infection, and acute fatty degeneration of the cells occurs.

Naked-Eye and Microscopical Appearances of Fatty Degeneration.—*The Arteries.*—Fatty degeneration in this situation is not of importance clinically except when it occurs in the vessels of the central nervous system and retina, as it may in poisoning from phosphorus, etc., and in the grave anæmias, when it may lead to rupture and hæmorrhage.

The cells in the adventitia of the small vessels of the brain are the first to show fat granules collected around their nuclei. Fatty degeneration, though seldom met with in the middle-sized arteries, especially those

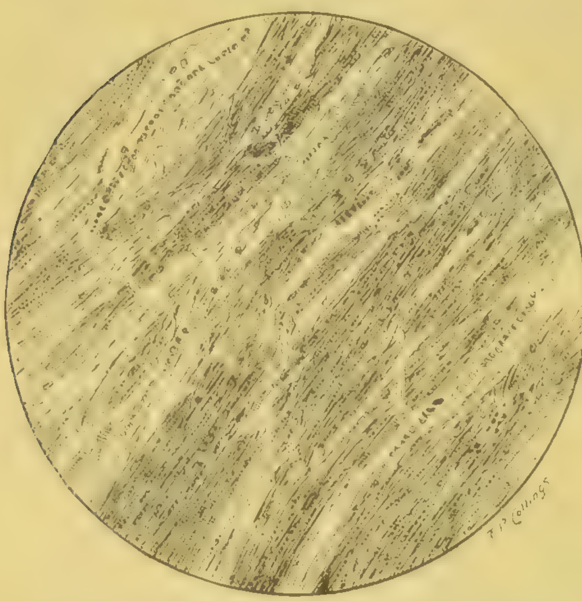


Fig. 43.—Photomicrograph of heart from a fatal case of diphtheritic paralysis, stained by the Marchi method, showing *early* fatty degeneration. The fine *black granules* in the fibres are particles of fat stained by the osmic acid. × 250 diameters.

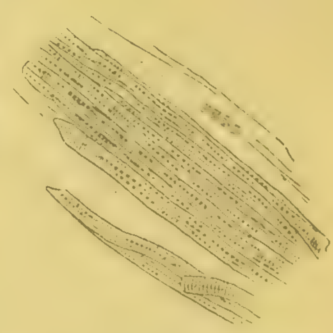


Fig. 44.—A few fibres more highly magnified.

of the limbs, is very common in the aorta, occurring as opaque, whitish streaks or spots scarcely, if at all, elevated above the surface. The fatty change occurs in the stellate cells of the subendothelial coat; and the tissue thus degenerated may give way so that a very shallow breach of the lining surface is produced.

The Heart.—As before said, the whole muscle-substance may be affected, or only the inner surface of the heart, which then assumes a peculiar pale, streaked appearance, seen especially in the musculi papillares and columnæ carneæ of the left ventricle, sometimes in the right ventricle, never in the auricle. This form of degeneration is produced by less severe nutritional defects of the organ; but when there is marked obstruction of the main branches of the coronary artery by atheroma,

idiopathic anæmia, or phosphorus poisoning, the general form of degeneration of the organ exists. The walls of the organ have a yellowish appearance instead of dark red; they are flabby, lacerable, and frequently present a "*tabby-cat*" or "*thrush-breast*" appearance. From a large experience in the examination of hearts, I am certain that fatty degeneration may be overlooked unless a microscopical examination be made after staining with osmic acid. Thus, in a case of fatal syncope occurring in diphtheritic paralysis, I found the organ extremely degenerated; yet the heart had been passed as normal on macroscopic examination. It was rather pale and tough, but, examined microscopically, the muscle-fibres were found to be extremely degenerated: the toughness was possibly due to coagulation-necrosis.

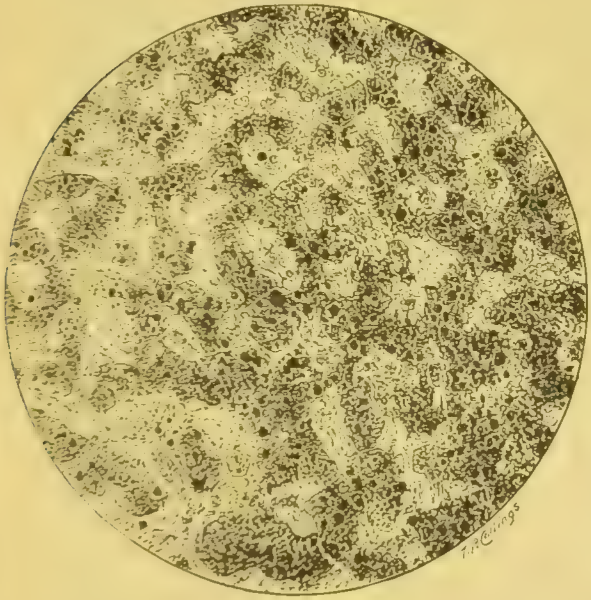


FIG. 45.—Photomicrograph of a section of liver, from a case of pernicious anæmia, stained by the Marchi method. The *black granules and droplets of very varying size* seen within the liver cells consist of fat stained by the osmic acid. × 300.

FIG. 46.—A few cells much more highly magnified.

Microscopical Changes in Fatty Degeneration of Muscle-Fibres, etc.—The fat granules occur first as fine molecules scattered through the fibre; only in advanced cases do they run together in droplets, and even then they never form drops (*vide* Figs. 43 and 44). At first the muscle-fibres do not lose their striation, but as the process advances the striæ become less marked, until eventually they may be entirely lost. Obersteiner has recently described a peculiar form of interfibrillary fatty degeneration of the muscles of the tongue in a case of tabes dorsalis: the hypoglossal nucleus was intact. In the liver cells and renal epithelium the fat droplets vary greatly in size, from fine granules up to drops which nearly fill the cell; so that it is sometimes extremely difficult to

determine whether the liver cells show fatty infiltration or degeneration (*vide* Figs. 45 and 46).

Fatty changes in the kidney are common, due to secondary degeneration of the epithelium and inflammatory products, *e.g.* large white and small white kidneys. Primary fatty degeneration of the cells of the liver and kidney occurs in phosphorus, arsenic, and antimony poisoning, especially in the first-named. Fatty degeneration may accompany lardaceous disease.

As the cells of the fixed tissues may undergo fatty metamorphosis, so may the cells of fluids, *e.g.* pus-cells; and of coagulated fluids, *e.g.* casts. It was once believed that fatty degeneration was the same process as the formation of adipocere, but Kraus has shown that aseptic tissues can be kept a considerable time without appreciable increase of fat. *Adipocere* is the result of the action of living organisms upon dead tissues, like the ripening of cheese; here compounds of the fatty acid series—caprylic, caproic, and butyric acids—are formed which unite with ammonia and alkalis to form soaps; whereas in fatty degeneration a neutral fat is formed.

Fatty degeneration occurs in atheroma (*vide* article "Diseases of Arteries") The *arcus senilis* is usually considered a sign of degeneration. It was formerly thought to be a fatty degeneration occurring in the cornea; but it is shown to be a deposit of matter (fat or colloid material staining black with osmic acid) in the lymph-spaces. It very probably comes from elsewhere; as it has been met with in fat young women, it is not a definite sign of degeneration. Fat in cells or tissues can be recognised microscopically by the colourless, highly refractive droplets with a dark contour, insoluble in acetic acid, soluble in alcohol and ether. They stain black with osmic acid or red with Sudan III. There is no reliable means of distinguishing fatty accumulation within a cell from fatty degeneration. In the latter stages of fatty degeneration, when the cells are dead and in great part destroyed, the whole tissue may be broken down into an opaque yellowish-white detritus such as occurs in atheroma. In the débris are found characteristic crystals of cholesterin—rhombic in shape, with a corner notched out—and feathery crystals of margarin.

Cloudy swelling, *parenchymatous or granular degeneration or albuminous*

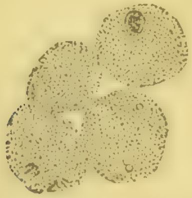


Fig. 47.—Cloudy swelling of liver cells (× 350 diameters).—*Hamilton.*

Fig. 48.—Same treated with acetic acid.—*Hamilton.*

infiltration, often precedes fatty degeneration, and was first described by Virchow as affecting the special cell-elements of organs in a state of paren-

chymatous inflammation. It is a chemical and structural change in the protoplasm of the cell, or fibre, which becomes swollen and indistinct in outline and structure; the nucleus also is obscured by the precipitation of fine granules of an *albuminous* nature (*vide* Figs. 47 and 48). These granules are feebly reactive to light, hence dusky in appearance; they are not stained by osmic acid, nor are they soluble in ether, but they dissolve in dilute acetic acid and caustic potash: they cannot be fat therefore, although fat granules often coexist as the morbid process advances. It occurs with especial frequency in the specific fevers—typhoid, diphtheria, scarlet fever, etc.—and especially affects the liver, kidneys, heart, and voluntary muscle-fibres; but probably all protoplasmic structures suffer. The change is not due to the pyrexia *per se*, but in all probability to the action of the toxins causing the fever. Cloudy swelling is the first change noticeable in poisoning by phosphorus, arsenic, antimony, carbon monoxide, and the mineral acids, thus preceding the fatty degeneration. To the naked eye the organs appear swollen and frequently anæmic; the tissue often has a lustreless appearance, but it is softer than natural. The change is well marked in the liver, but its most serious effect is upon the heart: the muscle-fibres become slightly opaque, pale, soft, finely granular, and their striæ indistinct; such a condition is frequently found in acute myocarditis.

In acute desquamative nephritis the epithelial elements of the uriniferous tubules, especially of the cortex, undergo cloudy swelling which terminates very often in fatty degeneration.

Calcareous Infiltration.—The blood, the lymph, and most of the tissues of the body contain lime salts; two-thirds of the weight of bone is made up of earthy matter. Calcareous deposition in a tissue may, therefore, be due to precipitation of the lime contained in the tissue, to precipitation of lime normally contained in the blood and lymph, or to excess of lime circulating therein, derived from disintegrative processes occurring in bone (*e.g.* caries, osteomalacia, or senile atrophy). Deposition from this last cause is termed metastatic.

Calcification of a tissue is most frequently a sign of *senescence*; it occurs generally in dead or dying tissue. It is not, however, exclusively an attribute of old age, for it has been known to occur in early life or childhood; a remarkable case has been described of calcification of the middle-sized and smaller arteries in a lad the subject of dorsal caries; calcification does not indeed necessarily depend upon the age of the part, as it may occur in the fœtal tissues of the placenta. It is very prone to occur in dead tissue, and Litten has shown that the process of calcification is intimately associated with coagulation of the albumin of the tissue. "If the renal artery of an animal be ligatured, and the ligature removed after an hour and a half, so as to allow the circulation to return, the only noticeable change is an exudation of albuminous substance into the Malpighian bodies. When the blood has continued to flow for twenty-four hours there is a precipitation of calcareous salts to such an extent that the organ may become as hard as stone."

Calcareous deposits contain calcium phosphate ($Ca_3 2PO_4$), traces of carbonate, and minute quantities of magnesium phosphate and carbonate —sometimes very minute quantities of fluoride of calcium and oxide of iron. The mineral matter, therefore, corresponds closely with that of bone. Calcified tissues are readily distinguished from true bone by the fact that when acted upon by HCl and the lime salts thus dissolved out, bone-corpuscles and lamellæ are seen to be absent.

Appearances: (1) *Macroscopic Examination.*—Calcified tissue often feels and looks like bone; it breaks with an irregular surface, and presents a yellowish and greyish aspect; this is the case when it occurs in plates or spicules, but from simultaneous fatty degeneration of the tissue it may have a mortar-like appearance and consistence: small whitish or yellowish concretions of varying size and form may be seen and felt in the soft detritus (*e.g.* in caseating glands and atheroma).

(2) *Microscopic Examination.*—The infiltration of the lime salts occurs both within the cells and in the intercellular substance, especially in the latter situation, where they first make their appearance as a fine precipitate of opaque, round, or irregular granules, which look black by transmitted light. As the process advances these increase in number, until ultimately the structure of the tissue may be lost. Thus portions of tissue may be converted into masses having a black, irregular outline and a homogeneous, glistening appearance. Usually the cell-elements of the tissue are enclosed and obscured by the precipitated lime salts; but in some situations (*e.g.* the brain) the ganglion-cells are the seat of deposition. The deposition within cells is best studied in this situation. The granules look like highly refractive particles, and are soluble without development of gases in HCl. The nucleus remains free from the deposit, but gradually diminishes in size as the lime accumulates within the cell. The dendrons are often affected, the neuron very seldom. Calcification of the ganglion-cells has been found in fractures of the skull; it is not due, however, to excess of lime in the blood (metastasis) so much as to death of the nerve-cells and alterations in the circulation.

Causes of Calcareous Precipitation.—If the lime salts be held in solution by the carbon dioxide present in the blood and lymph, then lowered metabolism of the tissues and enfeebled circulation, such as occur in senile decay, would by default of carbonic acid favour precipitation of the calcareous salts of the lymph; there is some evidence in favour of this hypothesis: arteries are extremely liable to calcification of their walls, veins are not. Incrustation of the walls of the left heart is common, of the right heart not; calcification of the renal glomeruli which normally contain arterial blood is common. Since the CO_2 tension in the pulmonary veins is extremely low, and yet calcification is never seen in them, there must be other factors which cause precipitation of the lime salts in arteries; such are all conditions which lower or destroy the vital endurance of the tissues forming the walls—occupations involving mechanical strain, diseases associated with high arterial tension, toxic conditions of the blood (*e.g.* alcohol and syphilis), and, lastly, old age.

Calcification is very liable to occur in dead, dying, or decaying tissues; it is often found associated with or following *fatty degeneration*, especially caseation; *e.g.* atheroma, caseous tuberculous glands, caseating foci in the lungs, and old infarcts. Many new growths undergo calcification in the centre, where nutrition is impaired, *e.g.* fibro-myomas of the uterus, psammomas and endotheliomas of the dura mater, carcinomas. Calcification of old inflammatory products, especially when occurring on serous membranes, is not uncommon; and we can thus account for the calcareous plates met with in the pleura, pericardium, and peritoneum. The muscular walls of the heart and granulations resulting from valvular endocarditis often are the seat of calcareous deposition; phlebolites of varicose veins are probably calcified granulations or thrombi. Dead tissues lying in the midst of living tissues are prone to calcification and *petrification*, *e.g.* lithopædium of extra-uterine gestation.

Calcareous infiltration occurs in process of time in abnormal or vitiated secretions of organs. Calcareous concretions are thus met with in the salivary glands, pancreas, tonsil, articulations, and synovial sheaths; and in the interior of cysts (particularly colloid cysts) of the thyroid and kidney.

Results.—As a rule calcification is associated with death of the tissue and loss of function; it is not a cause, but an effect, and always means lowered vitality if not death of the tissue. Calcification of muscle-fibres does not necessarily mean necrosis, but it indicates great depression of function.

Calcareous deposition may be salutary, *e.g.* when calcification of the inflammatory products surrounding parasites (such as trichinæ of muscle and echinococcus of the liver) encapsulates the parasite, and either renders it inert until the capsule is dissolved in the stomach of another animal, or until it is actually infiltrated with lime and destroyed.

Calcification of the cartilages of old people is not at all uncommon; it is met with in the larynx, trachea, and rib cartilages; it is, however, a provisional process prior to ossification. Likewise inflammation or disease of cartilage may be followed by vascularisation and ossification. The comparatively frequent occurrence of bony ankylosis in old people proves clearly enough that if the joints once become fixed from pathological causes, ossification of the articular cartilages will occur.

Pigmentary Infiltration.—The pigments found in the tissues are—(1) Intrinsic—those which normally exist in the body or arise from pigments already in the body. These pigments are either derived from the colouring matter in the blood—*hæmatogenous*, or are *non-hæmatogenous*.

(2) Extrinsic—those which enter the body by the lungs, skin, or alimentary canal.

A pigment containing sulphur, and probably non-hæmatogenous, is a normal constituent of the skin in some races and individuals, and consists of blackish or brownish granules contained in the deeper cells of the "rete Malpighii." In certain circumstances this pigment is increased; for instance, round the nipples in pregnancy and in parts of

the skin exposed to the air, and especially to the sun's rays. Intensification of the normal pigment of the skin is met with in certain pathological conditions; notably in Addison's disease, sclerodermia, leprosy, tuberculosis, and the cancerous cachexia. In wasting diseases generally the fat has a deep yellow colour, and the muscles assume a deep brownish-red appearance, due to intensification of the normal pigment. The pigmentation of the skin in Addison's disease, in leprosy, and in sclerodermia is probably due to changes in the nervous system (*vide* special articles). Leloir has shown that an atrophy of nerve-fibres occurs in parts affected with vitiligo. According to Unna, the epidermis may take on a brown colour by *keratinisation*, a process in which water and oxygen are taken from the cells, and the sulphur relatively increased thereby. He thus accounts for the pigmented appearance presented by the skin in ichthyosis and xerodermia.

Hæmatogenous pigmentation.—A certain number of pigments met with in the body are certainly derived from the blood-pigment, viz. the bile-pigments, bilirubin and biliverdin, urobilin (which is identical with hydrobilirubin), and hæmatoidin. All these pigments are iron-free, and give a play of colours with fuming nitric acid. When blood-corpuscles undergo destruction, as in large extravasations of blood, two substances may be formed—(*a*) *Hæmosiderin* and (*b*) *Hæmatoidin*. The former substance, containing iron, turns black with ammonium sulphide, and gives the prussian blue reaction with ferro-cyanide of potassium acidulated with hydrochloric acid; it takes the form of granules of varying size which are frequently found within leucocytes. Hæmosiderin may also be found in the renal epithelium, in the fixed cells of the connective tissue, and also in lymph-channels and lymphatic glands, whither it is carried by leucocytes. Organs which are allowed to undergo putrefaction, and contain a large quantity of hæmosiderin, turn black from the formation of sulphide of iron. This often happens in pernicious anæmia, where a very large amount of this substance is found in the liver owing to disintegration of the red corpuscles. Hæmosiderin in large quantities may be found in the liver and spleen in severe forms of malaria, owing to the destruction of the red corpuscles, and from the action on the blood of certain poisons, such as arseniuretted hydrogen and toluylenediamine. "In the peculiar condition of disease known as general hæmochromatosis, this iron-holding pigment is very widely distributed in the body, and is present in enormous amounts. Doubtless the excessive destruction of blood is essential to effect such depositions of iron, but it is clear that other factors of unknown character must also be in operation, since only a much more moderate deposition is occasioned by the most active blood destruction observed in states like pernicious anæmia, or in poisoning by blood-destroying drugs like toluylenediamine" (Herter).

Hæmatoidin, a pigment which is iron-free, may be formed from extravasated blood, *e.g.* in apoplexy. The brain-substance in the neighbourhood of the hæmorrhage is stained an orange-red colour, and microscopical examination reveals minute orange rhombic plates or granules of hæma-

Fig. 1. *Haematoidin Crystals from old haemorrhage into the brain × 400 Diams.*

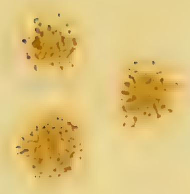


Fig. 2 *Haematoidin granules in liver cells, Cyanotic atrophy of liver × 400 Diams.*

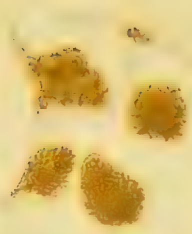


Fig. 3. *Cells from a melanotic sarcoma × 400 Diams*

Fig. 4. *Entraneous pigmentation Particles of coal & soot from a coal-miner's lung along with some pigmented catarrhal cells × 400 Diams*

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toidin. The deposit of pigment in the skin from changes in the extravasated blood is the cause of the characteristic colour of syphilitic eruptions and ulceration. Mr. Treacher Collins has shown that hæmorrhage into the anterior chamber of the eye is followed by a rusty staining of the cornea, due to imbibition by osmosis of blood-pigment, and conversion of the same into its derivatives *hæmosiderin* and *hæmatoidin.*

In malaria, in consequence of the hæmolysis induced by the malarial parasite, two kinds of pigments are formed: a pigment contained within the organism itself, black in colour, which does not give the iron reaction; another, hæmosiderin, found in the liver, spleen, and bone-marrow.

Melanin is a pathological pigment which does not arise from the blood; it can only be formed by the action of living protoplasm, and melanotic tumours are found usually to have originated in some tissue the cells of which normally contain pigments, *e.g.* the uveal tract of the eye. Melanin contains no iron, it has a black appearance in mass, but examined microscopically by transmitted light it is of a brownish or sepia colour; it is soluble in alcohol, ether, mineral acids, and solution of caustic potash, and is bleached by chlorine; these tests serve to distinguish granules of melanin from particles of carbon, etc. (*vide* Plate VII.).

Various pigments are found normally in the cells of the central nervous system, *e.g.* the locus cæruleus and locus niger; and the ganglion-cells of the brain, spinal cord, and sympathetic ganglia of human adults contain a fuscous pigment which occurs in the body of the cell, usually in the neighbourhood of the nucleus. This pigment is seldom present in children, and I have not been able to find it in monkeys and other animals. In young adults it is of a bright yellow colour; in old people it is darker and usually more abundant; it stains black by the Marchi method, and is therefore a fatty derivative. Whether it be really increased in certain diseases, or only more evident on account of atrophy of the rest of the cell-substance, we do not yet know; in progressive muscular atrophy many of the cells appear infiltrated throughout with pigments.

Pigments derived from extraneous sources are introduced into the tissues of the body by the respiratory and alimentary systems. *Anthracosis* is the pigmentation of the lungs and bronchial glands caused by the inhalation of fine particles of carbon which are taken into the lymphatics by leucocytes. Most adults have their lungs somewhat pigmented from this cause, but when, owing to occupations such as coal-mining, etc., enormous quantities of coal-dust are inhaled, the lungs may be absolutely black in colour.

Argyria, a condition of bluish discoloration of the skin, was occasionally seen in times gone by when nitrate of silver was used for long periods in the treatment of epilepsy.

HYPERTROPHY.—An organ is said to be hypertrophied when all parts of it undergo an abnormal increase, not due to degeneration or to

elements foreign to its normal structure. The term hypertrophy should not be applied to malformations, such as a large finger; or to excessive development of the organism as a whole, the result of congenital influences; but rather to "the enlargement of an organ, partial or complete, beyond its usual limits as the result of increased function or of some unusual condition of the corresponding or correlated organ" (Bland Sutton). Hypertrophy should, moreover, be distinguished from simple over-growth, as of uncut hair or nails.

Without increased blood-supply to the part hypertrophy cannot take place, but increased functional activity implies increase of nutrition brought about by vaso-dilation; this in its turn is induced by the stimulus acting on the vasomotor nerves of the small arteries. In glands there exist definite vaso-dilator nerves; when the gland is active the vessels dilate by the excitation of these nerves.

Functional and Compensatory Hypertrophy.—The increased size of a hypertrophied organ may depend upon two factors; namely, numerical hypertrophy or hyperplasia, and simple hypertrophy or the increase in size of its constituent elements. The two may go hand in hand; for example, the development and increased size of the muscles used in particular occupations or exercises are the result of an increase in size of the fibres due to increased nutrition. "Work-hypertrophy" is a natural attribute of working organs.

Another example of physiological hypertrophy is the gravid uterus, wherein muscular fibres of the organ increase both in number and in size. Kölliker showed that these unstriped muscle-fibres are eleven times longer and four times broader than in the normal state.

Compensatory Hypertrophy in Disease.—Of this there are many familiar examples. In dual organs—as the kidneys, testicles, lungs, and ovaries—when, from congenital absence, from disease, or from removal of one of the pair, the whole of the particular function is carried on for some considerable time by the other, the latter undergoes compensatory hypertrophy. Hollow viscera with muscular fibres in their walls afford examples of hypertrophy of muscular substance; *e.g.* the walls of the cavities of the heart undergo compensatory hypertrophy when increased functional activity is demanded by increased resistance in front: such is the hypertrophy of the left ventricle in chronic Bright's disease, and of the right ventricle in pulmonary obstruction and mitral stenosis. The hypertrophy of the left ventricle in aortic regurgitation may be explained by the increased functional activity and proportionally increased quantity of blood driven into the coronary arteries at each systole. Hypertrophy of the muscular coat of the bladder in stricture of the urethra, of the stomach in pyloric obstruction, of the intestines above a permanent stricture, serve as further examples of compensatory hypertrophy of hollow viscera.

Enlargement of the left lobe of the liver, when the right has been destroyed or its growth checked, is an example of *partial hypertrophy* of an organ.

An increase of the lymphatic glands after removal of the spleen affords an example of compensatory *hypertrophy of a correlative structure.* Two factors are concerned in all these functional compensatory hypertrophies: increase of nutrition, owing to increased blood-supply, and the physiological stimulus which excites the constituent cells or fibres of the organ to assimilate more nutriment. A cell is not nourished, but nourishes itself.

The forms of hypertrophy so far described may be looked upon as beneficial—even as physiologically normal; but examples of hypertrophy occur which are essentially abnormal. I can but allude to a number of curious pathological forms of hypertrophy, namely, leontiasis ossea of Virchow, which is characterised by multiple hyperostoses of the face and cranium; osteitis deformans, in which there is general increase of size with a marked morbid change of structure, in the form of a curious combination of condensation and hardening with softening and rarefaction; hypertrophic pulmonary osteo-arthropathy, a curious disease described by Marie. Hypertrophy, or perhaps a pseudo-hypertrophy of the pituitary body, is frequently associated with an enlargement of certain parts, especially the hands, the feet, and lower part of the face, due to an osseous proliferation and new formation of spongy bone (*vide* art. "Acromegaly," vol. iv.). The causes antecedent to these peculiar morbid hypertrophies are not understood. It is possible that some are due to the irritation of living organisms: for microbes may act upon animal cells, not only in a destructive manner, but as formative stimuli.

Friction or pressure, giving rise to hyperæmia of the cutis vera, causes increased proliferation of cells in the epidermis; but certainly this hyperplasia would not occur if the nerves to the part were destroyed. The irritation of the nerve-ending serves not only to determine an increased flow of blood to the part, but also increased formative activity on the part of the cells of the rete Malpighii.

Increased blood-supply to a limb may cause lengthening of a bone, of which an epiphysis remains ununited. Further, chronic venous obstruction leads to excessive transudation from the blood; this does not give rise to hypertrophy of muscular or glandular tissues, but to a fibrous hyperplasia which, as it progresses, may lead to shrinking of the organ at the expense of the essential cell-elements. In obstruction to the return of lymph from a lower limb, as in elephantiasis commencing in infancy, the limb not only increases in bulk generally, but relatively to those of the opposite limb, the bones become manifestly augmented both in thickness and in length.

Hypertrophy of bone has also been produced experimentally in animals by prolonged administration of small doses of phosphorus; this effect has been attributed to diminished waste, but it might also be explained by this substance acting as an irritant, thereby causing increased formative action. "Hyperplasia" is applied only to increased growth of pre-existing elements, normal in type and situation. Regeneration can only occur when matricular cell-elements still exist to

proliferate, and it must be borne in mind that highly specialised cell-structures—*e.g.* muscle, glands, and the central nervous system—show very little power of regeneration when injured. It is especially the fibrous connective tissues and epithelial tissues which possess capacities of proliferation and regeneration. Large areas of epithelium may be destroyed and yet regeneration occur; thus *skin grafting* is a familiar example of the inherent formative activity of the cells of the epidermis.

Cartilage offers an example of a non-vascular connective tissue which is incapable of self-repair; losses of substance are filled up by fibrous tissue. The periosteum, on the other hand, may be looked upon as the best example of the regenerative capacity of fibrous tissue.

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THE GENERAL PATHOLOGY OF NEW GROWTHS

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New growths or tumours have always strongly attracted the attention of pathologists. Their diversity of form and structure, the mystery of their origin, and, above all, the terrible toll which they exact upon human life, readily account for the fascination of their study. This study has been approached from the most various aspects. The clinical course and gross morbid anatomy of new growths have been carefully investigated for centuries past. With the introduction of the microscope their minutest structural details have been laid bare, and although histological technique has certainly not attained finality, it is improbable that any striking new discoveries await us from this standpoint. In recent years biologists, cytologists, bacteriologists, chemists, embryologists, and statisticians have attacked the problem, each from their own particular point of view. Direct experimental efforts at the artificial production and propagation of tumours have been numerous and sometimes even successful; but despite the vast amount of labour which has been bestowed upon the matter, it must still be confessed that the causation and actual nature of new growths are beyond our certain grasp.

The Meaning of the Term "New Growth."—Although it is by no means easy to frame a satisfactory definition of the term, our conception of what is meant by a "new growth" is now fairly definite. We do not

include under it all new formations of tissue: thus the hypertrophies are excluded, and also, though it is not always easy to draw a hard and fast line, inflammatory tumours, such, for example, as the infective granulomas. These are excluded on the ground that in such cases the newly formed tissue is functional, and that its function is directed to the service of the body as a whole. A new growth, in the restricted sense which is now current, *is a new formation of tissue exhibiting a greater or lesser degree of physiological independence, and conducting itself with no regard to the advantage of the organism in which it occurs.* This conception of a new growth is a comparatively modern one; it is not found in the classical work of Virchow, whose point of view was essentially morphological, but it is a conception of such fundamental importance that it must be considered in some detail.

The comparison of the animal body with a social community is sufficiently familiar, and has been elaborated in a well-known essay by Herbert Spencer. The structural units of the normal body, however diversified they have become in morphological and functional detail, work together in harmony for the good of the whole organism. Every cell lives its own life, but its individuality is subordinate. Definite law and order are manifest in the development of the body, in virtue of which suitable numbers of cells devote themselves to the several necessary functions in just that proportion which ensures the average well-being of the whole. The growth and maintenance of the tissues are secured by the orderly development of the appointed cells; the extent of each tissue is adequate to the immediate or prospective needs of the organism and no more. No cell, no tissue, no organ lives for itself alone; the resemblance to an ideal socialistic community is complete.

The very essence of a new growth lies in the absence of such subordination, and has been happily expressed by Thoma in the single word "autonomy." Tumours arise from the abnormal, disorderly, even riotous growth of certain tissue-elements which have in some way freed themselves from the restraints imposed by normal tissue-interdependence. The mystery of new growths might be solved could we but trace the process which has led to this revolt. The degrees of autonomy presented by different types of tumour vary within wide limits. In some extreme forms the anarchy of the cells is complete: in the more malignant types of sarcoma, for example, there is little attempt at the formation of a definite tissue; we see nothing but wanton cell-proliferation, with wholesale invasion and demolition of the normal structures of the body. Such a tumour as a lipoma contrasts strongly with this, the tissue of which it consists corresponds closely with normal fat; the growth passively increases in a sluggish fashion, but it does not aggressively invade the adjacent tissues; at the most it pushes them aside. Its autonomy is veiled and inconspicuous, becoming manifest only when an emergency arises. Normal adipose tissue is a reserve of hydrocarbon, to be utilised by the more active tissues when need demands; but it is an old observation that in starvation or fever a lipoma does not waste proportionally

with the rest of the subcutaneous fat; it shows its independence by refusing to share with the body in the hour of trial.

Normal tissues and organs, when they have attained the dimensions requisite for the due performance of their functions, cease to grow. They have not lost the power of growing,—witness the hypertrophy of a kidney, when its fellow is damaged or destroyed,—but the growth of normal tissues has a sort of natural limitation, ordained in the interests of the whole of which they form a part. When physiological equilibrium has been attained, it is reasonable to imagine a sort of mutual restraint exercised by the different cell-groups one upon another. In the case of tumours this restraint—this natural termination to growth—is largely wanting. Some grow fast, others slowly, but the general tendency is for a tumour to go on increasing in size, though some ultimately become stationary.

Of the various attempted *definitions* of the term "new growth" perhaps the most acceptable is that of Ziegler, according to whom a true tumour is "A new formation of tissue which appears to originate and grow independently, is atypical in structure, subserves no useful purpose to the whole economy, and the growth of which has no typical termination." This definition has the merit of emphasising the essential autonomy of the true tumours, but it is open to the criticism that all tumours are not necessarily atypical in their histological structure, however atypical the growth itself may be as regards the general structure of the body. There are many innocent growths showing, in their microscopic details, an almost complete conformity with normal tissues. Nay, more—even malignant growths are not unknown which are practically indistinguishable from normal tissues, as in the instance of "thyroid metastasis" in the cranial bones. Further, it is by no means certain that the cells of new growths never serve any function useful to the body as a whole. The matter has been discussed at some length by Hansemann (24). He points out that in cancer of the whole of the pancreas, diabetes is rare, as if the altered pancreatic cells still provided their internal secretion. The same is true of cancer of the adrenals, as regards Addison's disease. But perhaps the most striking case in this connexion is one recorded by von Eiselsberg, in which, after extirpation of a malignant thyroid growth, tetany and cachexia appeared, vanishing when a metastasis appeared in the sternum. This, in turn, was extirpated, and the tetany recurred, persisting despite a second metastasis in the scapula; it seemed as if function still persisted in the first metastasis, but had been lost in the second. Ewald found iodine in a growth secondary to a malignant thyroid tumour. The retention of some sort of function by the cells of innocent growths is well established, but the point here at issue is the performance of a function useful to the rest of the body. It is probable that such functions are lost in proportion to the departure of tumour-cells from the normal adult type.

The Zoological Distribution of New Growths.—Although most of our knowledge has been derived from the study of tumours in man.

they are well known to occur in the lower animals. In domesticated mammals they are common, and it is probable that when attention is directed to the matter, they will prove by no means rare in animals in a state of nature. The Cancer Research Fund, in the first year of its work, reported on some 70 specimens of malignant growths occurring in vertebrates other than man, including examples from birds, amphibia, and fishes. The growths were found to be essentially identical with those occurring in man; they comprised both sarcoma and carcinoma of many different types.

The Clinical Course of New Growths; Innocent and Malignant Tumours.—From the clinical standpoint tumours fall into two main groups, according to their course and behaviour in the body. The one group, including tumours of the most diverse histological structure, has the following characters in common. The growth remains confined to its seat of origin, as a rule is sharply defined from the adjacent tissues, and is frequently enclosed in a definite fibrous capsule. It shows no tendency to invade the neighbouring structures, which are merely pushed aside as the tumour increases in size. Although such tumours may be multiple, they never give rise to secondary growths in the lymphatic glands or in distant organs. Hence they are called "*benign*" or "*innocent*" growths, because they have little tendency to shorten life. They may attain a great size and occasion much inconvenience to the patient, but it is only exceptionally, from an accident of situation, that they kill. A growth of this type, if arising within the cranial cavity, may destroy life by pressure upon important centres in the brain, even though of quite modest dimensions, whereas a similar growth in the subcutaneous tissue may attain an immense size with little but inconvenience to its bearer.

In the second group are tumours, almost equally varied in their histological detail, having in common characters of much more serious import. They are not sharply defined from the adjacent tissues, but spread into and destroy them by a direct infiltrating growth. More than this, detached particles of the tumour-tissue pass along the lymphatics, and, becoming arrested in the corresponding lymphatic glands, form the starting-points of secondary tumours. Or, entering the blood-vessels, such particles are conveyed to distant organs,—the liver or the lung,—and set up similar foci of new growth there, so that, in an extreme case, almost every organ in the body becomes infected by the growth. Tumours such as these are usually much more rapid in their rate of growth than innocent tumours, and the havoc which they work amply justifies the term "*malignant*."

The clinical grouping of new growths into innocent and malignant forms is well established, and the great majority of the tumours met with in practice may readily be assigned to one or the other category. Nevertheless it would be an error to imagine any hard and fast line between the two. It is not unusual for a growth to possess some, but not all, of the attributes indicating malignancy. There are certain

tumours, commonly included with the sarcomata, which may infiltrate the surrounding tissues, and which, if they reach the skin, ulcerate and fungate, sometimes forming masses of considerable size, but which do not give rise to secondary growths in the lymphatic glands or in distant organs. Such are the "myeloid" tumours of bone and the so-called "serocystic" sarcomas of the breast. Rodent ulcer, amongst the epithelial tumours, falls into the same group. They are sometimes spoken of as possessing "*limited*" or "*local*" *malignancy.* But, as a matter of fact, tumours are to be found presenting every conceivable gradation between innocence and malignance—from the hard fibroma, of which the surgeon can predict with confidence that, if completely removed, it will not recur, up to the small round-celled sarcoma which, even if freely removed in its earlier stages, has only too probably already infected the adjacent parts or even distant organs. It is not possible to classify tumours into distinct groups on this basis. Innocency and malignancy are attributes of certain types of tumour; that is all. Moreover, in spite of statements to the contrary, a primarily innocent tumour may form the starting-point of a malignant growth.

Morbid Anatomy.—Before the introduction of the microscope much had been learned as to the gross morbid anatomy of new growths, and much may still be made out with the naked eye alone. But the microscope reveals so much more that only the evident macroscopic features of tumours need be referred to here.

It can readily be determined that different tumours consist of very different tissues; some are composed of bone, some of cartilage, fibrous tissue, or fat. Some are complex, and built up of many diverse tissues, others of only two. The latter often resemble glandular tissue, having a spongy fibrous framework from which the softer part may be expressed. Of the simpler forms, consisting of one tissue only, some evidently correspond to normal tissues; while others, and these habitually of malignant character, are soft, brain-like, and unlike any natural structure in the body. The latter forms used to be called "medullary" or "encephaloid" growths. By suitable injection methods it may be shown that all, or nearly all, tumours are vascular; some scantily so, others very richly provided with blood-vessels.

The limits of a growth can usually be defined with the naked eye, or at least it can be determined whether or not it is infiltrating the tissues adjacent. In the case of most innocent tumours a fibrous capsule sharply defines the limits, and the growth has frequently so slight a connexion with neighbouring structures that it can be shelled out with the finger nail. On the surface of the body tumours may project as warts, and on mucous surfaces as "polypi," often attached by a very narrow stalk.

Some tumours are cystic. They may consist of nothing but a congeries of cysts, with little solid tissue, as in the common multilocular ovarian cyst. At times the cysts may be seen filled with solid intracystic growths sprouting from their walls. In other cases the cyst-formation may be merely incidental, a few cavities occurring in an otherwise solid

tumour. Such cysts may owe their origin to necrosis and softening, or to hæmorrhage; or they may arise from the dilatation of natural spaces such as ducts, glandular tubules, or lymphatic spaces.

Tumours may be single or multiple. The majority of innocent tumours are single, but this is a rule subject to numerous exceptions. Uterine fibroids are usually multiple, and glandular polypi of the intestine frequently so. One of the most striking examples of multiplicity in innocent tumours is furnished by the occasional development of large numbers of fibromas in the peripheral nerves. In all these cases the tumours arise independently, and more or less simultaneously: one tumour is not genetically connected with another, though doubtless they have some common cause. In the case of malignant tumours, which even more than innocent ones tend to be primitively single, the process of metastasis often tends to give rise to multiple secondary growths—here genetically derived from the primary one, which they resemble in their histological characters. It is, further, by no means unknown for growths of different kinds to be present in the body at the same time; tumours are such common pathological phenomena that one might expect such occasional fortuitous concurrences. A patient may present two different kinds of innocent tumour, or an innocent and a malignant one, the two having no evident connexion. Or the concurrence may not be accidental, a malignant tumour having originated in one of a number of innocent growths, *e.g.* rectal carcinoma in multiple polyposis. The combination of two independent malignant growths is naturally rarer because of the more rapid course of such tumours.

Morbid Histology.—The application of the microscope to the study of new growths has much enlarged our knowledge, and, indeed, histology forms the basis of modern classification. With each improvement in microscopical technique new facts have been brought to light, and the minute structural detail of all the different forms of new growth is now fairly well known. They are found to reproduce the features of practically every tissue in the body. In the case of innocent tumours this reproduction is usually a tolerably faithful one, though slight differences in the form and arrangement of the cells are common enough, and perhaps almost justify the term "atypical" as applied to the structure of tumours in general. The adipose tissue of a lipoma, the fibrous tissue of a hard fibroma, the unstriped muscle of a uterine fibromyoma, usually present no features by which they can be discriminated, histologically, from such tissues elsewhere. On the other hand, the adenomas of the kidney or liver fail to present a perfect picture of normal renal or hepatic tissue; the cells are more irregularly grouped, though still readily recognisable as renal or hepatic in nature.

Amongst the important generalisations which have been reached by the microscopic study of new growths, there are some which demand detailed consideration.

Innocent tumours, as has just been said, reproduce the characters of normal adult tissue with tolerable fidelity. The more perfect their

clinical innocence, the more closely does their tissue conform to the normal adult type. The tissue of malignant growths, on the contrary, presents divergences from this type which are often of an extreme degree, and the more extreme the greater the clinical malignancy of the tumour. The divergence is from the adult type of tissue, and is generally regarded as of the nature of a reversion to the embryonic type. It consists in a loss of that specialisation which characterises the adult cell, and a resumption of the indifferent characters of the earlier stages of development. It is natural to correlate this apparent morphological retrogression with the enormous power of multiplication presented by the cells of malignant growths—a power essentially inherent in embryonic tissue; nevertheless, we have no right absolutely to refer this excessive power of proliferation to the resumption of embryonal characters; we can only say that in the great majority of cases the two phenomena go hand in hand. It must, moreover, be borne in mind that there is no actual retrogression of the individual cells; it is only that the multiplying cells of a malignant growth fail to develop into adult tissue.

The matter may best be illustrated by concrete examples. There are epithelial new growths arising in the mucous membrane of the rectum which are perfectly innocent in character, viz. the glandular polypi. Histologically, these correspond very closely to the normal mucosa of the part, being formed of orderly and perfect glandular tissue, with a supporting stroma of connective tissue and blood-vessels. The epithelium is columnar and perfectly regular in its arrangement; goblet cells are numerous, indicating that the cells are capable of their normal physiological functions. From this same mucous membrane malignant epithelial growths not infrequently arise, some growing slowly, others with great rapidity. Those which are of lesser malignancy consist essentially of epithelial cells, readily recognisable as columnar, and still so arranged as to form glandular tubes, resembling the crypts of the normal rectal mucosa. But the arrangement has little of the regularity seen in the innocent glandular polyp; the epithelial cells vary in size and shape, and some may already have begun to depart from the columnar form; their special physiological functions are in abeyance, if we may judge from the fact that only in very rare cases are goblet cells to be found in rectal carcinomas. In the more rapidly growing and more highly malignant rectal carcinomas even these resemblances to the normal mucosa are lost, and lost the more completely the further advanced the case. The epithelium is no longer of recognisably columnar type, or, at the most, is only here and there so recognisable. The majority of the cells are rounded or irregular in shape, and though they are still grouped in an alveolar fashion in the meshes of a scanty fibrous stroma, there is little to suggest the glandular tubes of the normal mucous membrane. The reversion of the cells to the primitive type is complete. What is true of the epithelial growths of the rectum holds good throughout all the series of new growths in other regions. The innocent tumours which arise from the connective tissues

present the structure of fully formed adult fibrous tissue, bone, cartilage, fat, and so forth. The malignant growths of similar origin present deviations from the normal in rough proportion to their degree of malignancy, culminating in the round-celled sarcoma—of all forms the most highly malignant—which represents the embryonal type from which all the adult connective tissues have been derived.

This change of type in the cells is conveniently denoted by the term "*anaplasia*," suggested by Hansemann (21, 22). Anaplasia means, etymologically, much the same as metaplasia, but the latter term is perhaps better restricted to the less fundamental type of change seen, for example, in the conversion of one kind of epithelium into another, as when, in procidentia uteri, the columnar cells become transformed into squamous under the influence of desiccation and mechanical attrition. The term metaplasia has the further disadvantage of association with the doctrine, now generally held erroneous, of the conversion of one sort of tissue into another totally different kind, *e.g.* of epithelial cells into connective tissue, and of connective tissue into epithelium.

The degree of anaplasia is, as has been said, roughly proportional to the malignancy of the tumour, though this is a rule not without exceptions. The fact may be expressed, according to current doctrines, in another way. The cells of a developing tissue have potentialities of two kinds: they have the power of multiplication, giving rise by mitotic division to daughter cells akin to themselves, and they have the power of individual development along their own special lines, whereby they become differentiated into normal adult tissue-cells. In the early development of the embryo the energies of the cell are chiefly directed to multiplication; in the latter stages they should be directed to individual differentiation and development. And as cells become more highly specialised they tend to lose their primitive powers of multiplication. It is not an unfair way of putting the matter to say that if the young cells of a new growth devote themselves to development along normal lines the result is an innocent tumour; as they become specialised into a normal adult tissue, they lose their embryonic faculties of multiplication, and hence their dangerous characters. But if they fail to develop along normal lines, remaining embryonal in type, they are apt to retain their primitive potentialities for multiplication, and malignancy is closely connected with the retention of this property. Anaplasia may be but the morphological expression of this physiological fact.

The foregoing considerations enable us, within certain limits, to predict the clinical course of a tumour from its histological characters. There are few problems so frequently set to the pathologist. As a general rule the answer can be given with some approach to certainty. The more histologically perfect and adult in type the tumour-tissue is found to be, the more likely is the tumour to prove an innocent one. The more unspecialised the tissue-elements, the more probable is it that it will run a malignant course. But he who would seek in all cases to pronounce a final verdict on histological evidence alone is doomed

to disappointment. It is always desirable and sometimes absolutely necessary to be informed as to the clinical history and macroscopic characters of a growth in order to interpret aright its histological features. The tissue forming the mass of a fleshy mole of the skin is very like sarcoma tissue; some malignant melanotic tumours originate in such moles, but the vast majority of moles remain throughout life perfectly innocent tumours. Yet it is not always possible to tell from their microscopic characters alone whether they are innocent or have already given rise to secondary melanomas. Again, some of the most virulent round-celled sarcomas are so like lymphoid tissue that without a knowledge of the clinical history and other characters of the growth one cannot say for certain whether or not it is malignant; the same is true of certain spindle-celled or mixed-celled sarcomas and granulation tissue. In 1903, however, it was asserted that there does exist one positive histological criterion of malignancy, namely, the presence of the "heterotypical mitoses" presently to be mentioned. It may be that this claim is justified, but the difficulty of demonstrating such mitoses is not inconsiderable, and it cannot be said that the facts at present available are sufficient to justify us in dogmatising upon the point.

Cytology.—It will be convenient at this point to consider the question of anaplasia in more detail, and especially in relation to cytology. There is little to call for remark in the cell-details of innocent growths. So far as is known, the cells forming these tumours present no marked differences from those of the normal tissues with which they correspond. The mitotic figures which are found in them are of regular configuration and of the ordinary somatic type. Malignant growths, on the other hand, exhibit certain cytological features of much interest, and possibly of much theoretical importance.

It has already been mentioned that the cells of malignant growths habitually show a reversion towards the primitive and unspecialised type from which, in the normal development of the embryo, they have descended. The change is often more conspicuous in recurrences and metastatic deposits than in the earlier stages of the primary tumour. From this it seems permissible to infer that it is truly a reversion from the higher type and not merely a persistence of embryonic characters on the part of the descendants of a group of cells. Anaplasia is seen only in the tumour-cells themselves, not in their incidental and supporting framework: the fibrous stroma of such as present an alveolar structure, *e.g.* the carcinomas, is habitually ordinary fibrous tissue, or, in the earlier stages, a granulation tissue with apparent potentialities of developing into adult fibrous tissue. So, too, the endothelium lining the blood-spaces of malignant tumours presents no evident differences from the endothelium of other newly formed capillaries. It is the sarcoma-cells or carcinoma-cells themselves which show the reversion. Such cells often present marked discrepancies in form and size. Not indeed always, for in the ordinary round-celled and spindle-celled sarcomas the cells are

generally fairly uniform; yet even here cells can usually be found which here and there stand out from the rest in virtue of their larger size, and bigger and more deeply staining nuclei. But in the majority of malignant growths the cells vary amongst themselves to a very striking extent; in sarcomas it is common to find spherical, oval, spindle-shaped, and irregular cells mixed up so indiscriminately that the term "mixed-celled sarcoma" is applied to them. In such growths it is usual to find individual cells much above the average in size, sometimes ten times as large as their fellows; such very large cells are frequently, but not always, syncytia with several nuclei. What is true of these sarcomas is true also of many rapidly growing carcinomas; the cells have not only reverted to a primitive type, but present considerable differences amongst themselves, both in the size and shape of the cell-body and in the number, form, size, and staining capacity of their nuclei. The large cells of rapidly growing tumours, apart from degenerative changes, are often vacuolated, and may contain considerable stores of glycogen and fat.

It is, however, in the nuclei of malignant growths that cytologists have found the widest departures from the normal. This is only what might have been expected, for it is an accepted doctrine that the nucleus is the controlling centre of cell-activity, and takes the essential part in constructive metabolism. In cells which are proliferating wildly and at random it is natural to expect nuclear anomalies, though we do not know whether these aberrations are the cause of the random growth or its consequence. In normal tissues, even though the cell-bodies may vary somewhat in size, the nuclei are commonly very uniform, and contain approximately the same amount of chromatin. In innocent tumours this is also the case. But in malignant growths it is not unusual to find an irregular distribution of chromatin, one cell containing perhaps twice as much as its neighbour, and hence showing a much greater staining capacity in its nucleus. The mechanism of this unequal distribution lies in the aberrant mitotic figures which are characteristic of malignant growths, and have in recent years attracted much attention.

It is quite clear that mitosis is the normal mode of cell-division in the healthy body. Direct or amitotic cell-division is an exceptional event, occurring when the series of divisions is nearing its end in cells on the way to degeneration. The object of mitosis appears to be an exactly equal division of the chromatin between the daughter cells; the chromatin collects at the equator of the achromatic spindle into a number of bent rods, known as chromosomes; each rod splits longitudinally, and one half of each passes to each daughter cell. The number of chromosomes is constant and characteristic for each species of plant or animal. The importance of the complex process is due to the fact that the nuclear chromatin appears to be the actual physical basis of inheritance. Nothing is more striking, in the process of normal cell-division, than the regularity and symmetry of the mitotic figures. Malignant growths afford the best-known instances of irregular mitoses. Such miscarriages of the

mitotic process may indeed be produced artificially by chemical poisons, but they are extremely rare except in malignant tumours. Even here they are usually uncommon in comparison with regular mitoses, but Hansemann (23), who has paid special attention to the subject, declares that he has never failed to find them on careful search. He classifies the mitoses found in malignant growths into three groups, according to the number of chromosomes present. They may be normal in this respect, "hyperchromatic" with an increased number of chromosomes, or "hypochromatic" with a diminished number. He further distinguishes (1) asymmetrical mitoses, in which an unequal distribution of the chromatin between the daughter cells is the essential feature, and (2) pluripolar mitoses, in which a polyaster is formed instead of the normal diaster. The latter anomaly depends upon the formation of several centrosomes and attraction spheres—three, four, or many,—and results in the formation of a corresponding number of daughter nuclei. In the case of the asymmetrical mitoses unequal centrosomes are presupposed, resulting in hyperchromatic and hypochromatic daughter nuclei. Hypochromatic cells, with a diminished number of chromosomes, may also arise by the straying or degeneration of some of the chromosomes.

In 1903 Farmer, Moore, and Walker announced a further discovery as regards the cytology of malignant growths, namely, the occurrence of heterotype mitoses. This form of mitosis had been described by Flemming in 1887. More recently it has been shown to possess a remarkable biological significance, being uniformly characteristic of the final series of cell-divisions which give rise to the male and female sexual cells throughout the animal and vegetable kingdoms. In heterotypical mitosis the number of chromosomes is reduced to exactly one-half of the normal somatic number. They undergo only partial fission, the two halves remaining attached by their extremities, and opening out into thickened rings, which become disposed longitudinally on the nuclear spindle, and finally divide transversely. In fertilisation each parent cell contributes half the somatic number of chromosomes, which is thus restored in the embryo, remaining constant till again in the development of ova and spermatozoa the heterotype form of mitosis recurs. Farmer, Moore, and Walker recognised this type of mitosis in malignant growths, and their observations have been confirmed by Drs. Bashford and Murray. Only a small number of the mitotic figures in a malignant growth are of the heterotypical form. In the growing edge only ordinary somatic mitoses are found. Further in occur scanty heterotype forms, with "homotype" mitoses, *i.e.* figures conforming to the somatic pattern, but with the reduced number of chromosomes. The theoretical significance of this discovery will be considered later. It is asserted that heterotypical mitosis occurs only in malignant neoplasms; in innocent growths it has not, so far, been observed, and, with one doubtful exception, it has not been seen in the stroma of malignant growths.

Amitotic nuclear division is occasionally seen in malignant growths, but its significance is not clear.

Drs. Bashford and Murray have further described a process of conjugation between the nuclei of neighbouring cells in implanted epithelioma in the mouse, a discovery which, if confirmed, is of great theoretical importance. They consider the phenomenon identical with that of conjugation in certain protozoa and lower plants, and they attribute to it the same significance, viz. rejuvenescence and the starting of a new cycle of growth. They point out that such rejuvenescence by conjugation would go far to explain the character of malignant tumours. It is evident that much caution must be observed in interpreting the appearances described. The cells of malignant growths readily take up into their interior foreign particles, leucocytes, and even adjacent malignant cells; a partially ingested cell might give rise to appearances suggesting conjugation. The final stages of division might also suggest the same thing.[1]

Histogenesis.—There is practically no tissue in the body the cells of which may not originate an autonomous new growth. All such tumours must of necessity arise from the pre-existing cells of one tissue or another—sometimes from more than one. They tend, as might be anticipated, to reproduce the characters of the special tissue from which they have arisen. Thus we find cartilaginous and bony tumours arising from bone, unstriped muscle, and fibrous tissue in uterine fibroids, and deeply pigmented sarcomas growing from the uveal tract of the eye. Carcinomas arising from different epithelial surfaces usually present, save where the degree of anaplasia is extreme, an indication of the special characters of the epithelium from which they have originated: for example, the cancers of the intestine are habitually columnar-celled, while those of the œsophagus and skin are habitually squamous-celled. Tumours which thus obviously reproduce the characters of their parent tissues are spoken of as "*homologous.*" Sometimes, however, it happens that a tumour possesses characters quite foreign to the tissue in which it apparently arises. Such growths are termed "*heterologous.*" It is probable that their heterology is often more apparent than real, and that in truth, when a cartilaginous tumour develops in the parotid gland, it arises not from true parotid tissue, but in a misplaced rudiment of cartilage which has by chance become included there, just as tumours of evident suprarenal type may originate in the kidney from the suprarenal rudiments which we know to be frequently present in that organ. It must, however, be borne in mind that in very many cases the histogenesis of a tumour is a matter of inference; the growth comes under pathological observation only at a late stage, when its primitive connexions are destroyed or obscured. This difficulty is particularly noticeable in the case of malignant tumours, and the more so the greater the degree of anaplasia.

Inasmuch as we can never witness, under the microscope, the actual

[1] By the courtesy of Drs. Bashford and Murray the writer has had the opportunity of examining the specimens, and is of opinion that the appearances do actually bear the interpretation claimed for them, of a true nuclear conjugation.

inception of a new growth, we cannot positively decide whether it in all cases has a single point of origin, or at times may have sprung up simultaneously at several independent points, as is evidently the case in multiple innocent tumours. Malignant tumours are often assumed to arise from a single point. Ribbert strongly argues this to be the case in carcinoma, and affirms that, where such a growth is continuous with the surface epithelium at several points, the continuity is secondary everywhere but at the one site of origin. The matter is one scarcely susceptible of proof or disproof; there seems no reason for doubting that a malignant growth may take origin from a single small group of cells, or, for that matter, from a single cell. What we do not certainly know is whether, having thus originated, the entire cancer thenceforward consists of cells lineally descended from the primitive cell or group of cells, or whether adjacent cells may undergo a similar "malignant transformation." The balance of direct evidence seems in favour of the first of these views. Nevertheless, cases certainly occur in which areas of epithelium in the vicinity of a carcinomatous growth, but having no evident connexion with it, appear to be undergoing the same change. That an organ such as the kidney may be entirely converted into a malignant growth, retaining the shape of the original viscus, is difficult to explain on the view of a single focal origin. This point will be discussed in more detail in considering the modes of growth of tumours. Surgeons habitually remove the entire breast when it has become the seat of even a small carcinoma, not only because they are afraid of not removing the whole growth, but also because a gland which has once originated a malignant tumour may do so again. Thus the writer has examined a case in which a small, well-defined tumour, removed from a breast, showed the structure of colloid carcinoma. After an interval of between one and two years the breast had to be removed on account of a cancerous growth of such totally different type, that ordinary recurrence seemed out of the question.

A new growth presents a stroma as well as a parenchyma. In the case of epithelial growths, both innocent and malignant, and in the so-called alveolar sarcomas, the distinction is very obvious. In the case of tumours of the "connective-tissue" type, including ordinary sarcomas, it is much less obvious. Yet even the most anaplastic sarcoma has at least a stroma of blood-vessels, and in the majority of cases some framework of supporting tissue can be distinguished, even though imperfectly differentiated from the essential parenchyma. The histogenesis of this stroma must, therefore, be considered. It may be taken as a general law that the parenchyma of a new growth develops from the parenchyma, and the stroma from the stroma of the parent tissue. At the growing edge of a carcinoma it can readily be seen that the tumour-cells intrude themselves into the spaces of the adjacent tissues, and are supported by these tissues, which are thus utilised as a stroma. In the case of metastatic malignant growths it seems sufficient that a group of parenchyma cells, or perhaps a single cell only, be transported to a distant organ; the

stroma in such cases is evidently formed from the stroma of the organ thus secondarily invaded, showing that the essential part of the growth is the parenchyma. A further source for the stroma lies in an inflammatory new formation of connective tissue. The majority of malignant growths appear, as they spread, to exert an irritant effect upon the neighbouring tissues, evidenced by the characteristic zone of small-celled infiltration around their margins. In the more rapidly growing varieties this phenomenon is inconspicuous, and there is no time for much permanent new formation of tissue in a zone which is ever shifting as the tumour extends. But in the more slowly growing types a marked reactive fibrosis may occur as the result of the chronic irritation, the newly formed fibrous tissue being itself slowly penetrated by the parenchyma cells of the tumour. Thus arises the type of cancer to which the term "scirrhus" is applied. Nevertheless it would be an error to imagine that in every case the stroma is derived locally from the pre-existing tissues of the affected area. In the metastases of some osteo-sarcomas calcification of the stroma is well marked, and indicates its derivation as an integral part of the growth.

The Modes of Growth of Tumours.—All tumours, innocent and malignant alike, tend to increase in size by *interstitial* growth, *i.e.* by the multiplication of cells by fission throughout the substance of the tumour. Direct evidence of this is seen in the common presence of mitotic figures, and of cells in all phases of division. The mitotic figures often occur in groups, suggesting foci of formative activity. In the case of innocent tumours this continuous local growth merely compresses the tissues adjacent, but in the case of malignant tumours a process of infiltration is seen in which the cells, multiplying at the margins of the neoplasm, insinuate themselves into the crevices of the surrounding tissues, thus gradually extending the limits of the mass. This, too, is classed as *continuous local growth*, but to it there is often added, in malignant tumours, a process known as *discontinuous local growth*, in which the tumour-cells are carried along the lymph-spaces for a short distance before they are arrested to form new islands of tumour-tissue in the immediate vicinity of the parent growth. Such islands soon become incorporated with the main mass as it extends.

Allusion has already been made to the question whether a malignant tumour owes its local spread solely to the multiplication of its own cells, or whether other cells of the mother-tissue adjacent can become converted into malignant cells. Different observers have placed different interpretations upon the appearances they have noted, and the matter is so largely one of inference, that no settled opinion can be said to exist. Some authorities, such as Ribbert, maintain that when a malignant growth has once arisen, its spread takes place only by the multiplication of its own cells; however widely it may extend in the body, every cell of which it consists is, on this view, a lineal descendant of the primary cells of the original malignant focus. In the very careful observations of Drs. Bashford and Murray on the course of implanted epithelioma in the

mouse, it appeared certain that the whole resultant tumour arose from the implanted cells. Others, as for example Hansemann (23), while admitting that this may often be the case, are unwilling to acquiesce in it as a universal rule, inclining to the belief that in some instances a "malignant transformation" takes place in adjacent cell-groups of the mother-tissue. In Hansemann's opinion, while a tumour may arise singly, even from a single cell, in other cases it may arise, simultaneously or successively, over larger areas, which may later coalesce. The writer has examined at least one case, an epithelioma of the penis, in which, in an area of skin adjacent to the primary growth, the cells of the epidermis had acquired anaplastic characters while still maintaining their normal anatomical relations, and having no apparent connexion with the primary growth. It is certain that, in the neighbourhood of a primary malignant tumour, the mother-tissue tends to undergo hyperplasia,—"collateral hyperplasia" of Hansemann,—and it may be difficult to draw the line between this and the growth itself. It is often maintained, probably with justice, that a "precancerous" stage of epithelial hyperplasia is antecedent to the actual development of cancer.

Metastasis.—The discontinuous local growth, mentioned above as occurring near the margins of malignant tumours, forms a transition to true "*metastasis*," the formidable property to which such tumours owe their chief terrors. By metastasis is meant the development of secondary tumours at a distance from the primary growth. Such metastatic growths are due to the detachment of cells, or groups of cells, from the parenchyma of the parent growth, and their lodgment elsewhere by a process of embolism. It is to be inferred from the close correspondence in histological structure between the metastatic and primary tumours (the only exception to which lies in the greater degree of anaplasia sometimes shown by the secondary growths) that the cells of the metastatic tumour are in all cases the lineal descendants of those of the original primary focus. There are two ordinary paths by which such transference of tumour-cells may occur, the lymph-channels and the blood-vessels. It may be stated as a general rule that in the carcinomas metastasis occurs chiefly by the lymph-paths, and in the sarcomas by the blood-channels. This rule is, however, subject to very frequent exceptions; it is not rare for sarcomas to affect the lymphatic glands; melanotic sarcoma, for example, frequently does so. Nor is it rare for carcinoma to give rise to distant secondary foci in the lung, liver, or bones, and, in the case of carcinoma of the intestine, metastasis by the portal vein is the rule. The reasons usually assigned for the different metastatic tendencies of the two chief forms of malignant disease are two in number. The blood-vessels in a sarcoma have a much more intimate relation to the tumour-cells than those of a carcinoma. In the former they are mere tubes of endothelium running naked amongst the sarcoma-cells; in the latter they run in the fibrous stroma of the growth. Hence, it is supposed, the greater readiness with which sarcoma-cells pass into the circulation. In the second place, it is alleged that sarcoma-cells are adherent to one

another by an intercellular material, while carcinoma-cells are but loosely attached; hence the latter are readily separable and pass freely into the lymph-spaces, whereas it requires the greater force of the blood-current to detach sarcoma-cells. Where the cells of a malignant growth gain access to a great serous cavity such as the peritoneum, extensive dissemination readily occurs, whether the growth be a sarcoma or a carcinoma.

The laws governing metastasis are hard to understand. It is strange, as pointed out by Virchow, that those organs which are common seats of primary malignant disease, such as the stomach, are rarely the seat of metastatic growths, while conversely the organs in which metastatic growths are common (lung, liver) are the very ones in which primary malignant growths seldom arise.

No necessary connexion exists between the size of the primary growth and the extent of its metastases. Enormous secondary growths may be disseminated throughout the body from a primary focus so small as almost to escape detection, as is sometimes seen in melanotic sarcoma arising from a small pigmented mole. It is often difficult to determine, after death, which has been the primary growth and which the secondary. Metastases are, as a rule, more sharply circumscribed than the primary tumour, and there is an absence of collateral hyperplasia in the adjacent tissues. Moreover, antecedent probability is a guide in many cases, whereby, from the histological characters of the growth and its known frequency of occurrence in any given organ, a fair guess can be made as to its primary origin. The apparent relative ages of the different tumours may also furnish a clue, even when no clinical history is forthcoming.

Recurrences.—When an innocent tumour has been completely removed by the knife it does not return. But in the case of a malignant growth there is no such certainty, and this for several reasons. The boundaries of a malignant growth are often ill-defined, so that the surgeon cannot be sure that he has taken it all away. Small outlying islets of discontinuous local growth may easily escape detection by the naked eye, while lymphatic glands or even distant organs may already have become infected. For these reasons the operations undertaken for the removal of malignant growths tend to become more and more radical, and the success of such operations as Halsted's seems certainly greater than that attending removal of the breast alone. Surgeons are also careful to avoid, where possible, any incision into the growth itself, lest its cells should escape and infect the wound. Finally, there is the possibility, when the whole of the affected organ is not removed, that an apparent recurrence is really the development of an independent growth in a tissue for some reason predisposed to such an aberration. It has been observed that successive recurrences of any given growth tend to show a higher and higher degree of anaplasia and malignancy.

Transplantation of Tumours.—If the cells of a malignant growth can be transported by metastasis to a distant part of the body, and can

found there a new colony of similar cells, it might be anticipated that a similar transplantation would sometimes occur directly, from a diseased to a healthy surface, by mere contact. Such direct inoculation has occasionally, though by no means commonly, been observed in human cases of malignant disease. Cancer of the vulva, commencing in one labium, may extend to the opposite labium without any actual continuity of growth, and an instance is often quoted in which an ulcerating cancer of the breast infected a paralysed arm which was in constant contact with it. Cases of inoculation of the glans penis from the os uteri have also been recorded, but must be received with some reserve.

Very numerous attempts have been made by different observers to transplant malignant growths experimentally from one animal to another. All attempts to inoculate a growth from one species of animal into an animal of a different species have proved fruitless. Numberless endeavours have been made to implant human carcinoma or sarcoma into the lower animals, but there is no authentic instance of success. Messrs. Shattock and Ballance (61) record experiments in which twenty-three carcinomas of the breast and six sarcomas were implanted into the peritoneal cavities, subcutaneous tissues, and muscles of monkeys, dogs, rabbits, rats, sheep, and cats. The pieces of growth introduced invariably underwent coagulation-necrosis, and were absorbed, encapsuled, or, in one case, calcified. The reason for this universal failure is probably to be sought in the existence of cytolysins, which destroy the foreign protoplasm, just as they would cause hæmolysis of the blood-corpuscles of an animal of another species introduced into the circulation. Where, however, similar experiments have been carried out between animals of the same species, in which no question of the introduction of a totally foreign protoplasm arises, success has often been attained. Hanau's experiments on rats are well known; from a rat which had a squamous-celled carcinoma of the vulva he inoculated other rats intraperitoneally and reproduced the disease. Velich says that he has been equally successful with a spindle-celled sarcoma from a rat, reproducing the disease on other rats through nine generations, though in guinea-pigs no effect was produced. Both Jensen and Borrel have been successful with carcinomas in mice, the growths being apparently capable of indefinite propagation in other mice, though only a variable percentage of the inoculations succeeded. In the first Scientific Report of the Cancer Research Fund Drs. Bashford and Murray record successful inoculations into mice with tumour material sent by Prof. Jensen from Copenhagen to London. They completely confirm Jensen's results. In spite, however, of these successful inoculations, it would appear that the majority of efforts at tumour transplantation, even within the limits of the same species, have been without effect. Amongst those which have succeeded must be included one example of an innocent growth, namely, the ordinary cutaneous wart. Jadassohn records numerous positive results on man by intra-epidermal inoculation, and Lanz was equally fortunate; the incubation period was a long one, amounting to several months.

Degenerative Changes in New Growths.—When compared with normal tissues, new growths are found to be far more prone to degenerative changes and actual cell-death. Nor is it hard to understand the reason for this. It is, as it were, the price which they pay for their autonomy. The life of a tumour-cell is a short, though an active one. The proper tissue-cells of the body are duly cared for in the interests of the whole organism, but there is no reason why the organism should do more than it can help for a parasitic growth which, it may be, is doing it irreparable damage. The cells of the new growth piratically appropriate what nutriment they can, but there is reason for believing, at least in the case of the malignant tumours, that their nutrition is defective. It may well be that with the assumption of anaplastic characters they have lost something of their assimilative powers, so that their available nutriment does them little good. It may be, as Hansemann suggests in the case of metastases, that the food provided for the normal organ is unsuited to the foreign cells which have intruded into it. Further, although most, if not all, tumours are provided with blood-vessels, many have but a poor vascular supply as compared with normal tissues. Lastly, on the view to be discussed later, that a tumour is a sort of abortive individual, it may be conceived of as having a naturally shorter span of life than a healthy organism. For these, amongst other reasons, it is not surprising to find new growths peculiarly liable to degenerative changes.

Fatty metamorphosis is the commonest form of degeneration in tumours, especially in the epithelial cells of carcinoma, and usually ends in the disintegration of the cell. Occasionally, where the fatty change is extensive and the cells die slowly, true *caseation* is seen, but it is uncommon in tumours as compared with the infective granulomata.

Infiltration with glycogen is a common phenomenon in rapidly growing malignant tumours, which, it is alleged, may contain an even higher percentage of this substance than the normal liver; the process is not a degeneration in the proper sense, but represents the accumulation of a food-reserve. Special methods are needed for its demonstration, but it is probable that some of the vacuolation seen in the cells of tumours represents spaces occupied in the fresh state by glycogen.

Mucoid degeneration is another common change in new growths. It may affect either the stroma or the cells of the parenchyma. In the case of the stroma the intercellular material swells up and becomes converted into mucin or some allied body. A fibromatous tumour may, in part or wholly, undergo this change; thus arises the growth known as a myxoma. A similar degeneration in some forms of sarcoma gives rise to myxosarcoma. Cartilaginous tumours may undergo central mucoid softening. In the case of the parenchyma of epithelial tumours, mucoid degeneration may occur in isolated cells, or may gradually involve all the parenchymatous elements. It is well seen in many ovarian cystomas, and is the essential transformation in so-called "*colloid*" cancer. From the chemical standpoint the term "colloid" cancer is a misnomer, for the substance

formed is not true colloid, such as occurs in the thyroid gland, but swells up in water, and is precipitated by acetic acid after the fashion of a mucin. The degeneration begins here and there in isolated cells; droplets of the mucoid material appear in the substance of their protoplasm and gradually coalesce, till presently the whole cell is converted. Ultimately all the cells in an alveolus may disintegrate into a uniform mucoid mass, in which no indication of the original cells is apparent. This tendency to mucoid transformation is most commonly seen in cancers arising from epithelium which has a physiological tendency towards the production of mucus, *e.g.* in the columnar-celled carcinomas of the stomach, intestine, and rectum, but it occurs also in other situations, such as the breast. Metastases from such growths may or may not exhibit a similar transformation.

Hyaline degeneration is not infrequent in new growths. It may affect the stroma, and is often seen in fibrous tumours. It occurs also in the cells of the parenchyma; sometimes the entire cell is converted into a homogeneous translucent mass, acquiring a strong affinity for acid dyes, while the nucleus disintegrates; at other times hyaline droplets appear in the protoplasm, or even in the nucleus. It is probable that some of the bodies which have been described as cancer-parasites (*e.g.* Russell's fuchsin bodies) are of this nature, *i.e.* localised areas of hyaline degeneration in the cell, with peculiar staining reactions.

Fibroid degeneration, or, more accurately, a process of replacement-fibrosis, is seen in some slowly growing cancers. In "atrophic scirrhus" of the breast the cancer-cells in the older portions of the tumour have commonly undergone complete atrophy, leaving only the dense fibrous stroma. The umbilication often seen in secondary cancerous nodules in the liver is partly traceable to cicatricial changes of similar nature in the central parts of the mass.

Calcification.—In old and hard fibromata, and in uterine fibro-myomas which have ceased from active growth, a deposit of lime salts is by no means rare, and may convert the entire tumour into a calcareous mass. Similar calcification may occur in cartilaginous tumours, and the central cells of the curious whorls of some meningeal endotheliomas may become the seat of calcareous deposit, giving rise to the growth known as "psammoma." The calcification which often takes place in the periosteal sarcomas is less a degenerative process than a sign of the inherent tendencies of the cells of the periosteum towards the deposition of lime salts, and in certain cases (true osteo-sarcoma) the tissue formed is of the nature of true bone, which may even be reproduced in the metastatic growths.

Necrosis.—Commonly enough the degenerative changes, to which the cells of new growths are liable, pass on to actual death of larger or smaller areas of the tumour. Such necrotic areas are very frequent in malignant growths, standing out as well-defined, opaque patches of a paler tint than the still living tumour-tissue. At times they may soften and break down, with cavity-formation. Uterine fibroids are liable to necrotic

changes, and indeed such changes are to be reckoned as frequent in many soft and rapidly growing tumours, which may even slough *en masse.*

Hæmorrhages, though not to be included as degenerations, are often associated with necrotic change. Section of a malignant growth frequently shows larger or smaller areas into which hæmorrhage has occurred, and remains of old or recent blood extravasation are often found on microscopic examination. Sarcomas, from the thin and unprotected character of their vessel walls, are specially liable to hæmorrhages. In the myeloid sarcomas of bone the combination of necrosis and hæmorrhage may convert the growth into a cavity filled with clot, and bounded by a layer of tumour-tissue so scanty that it may almost escape recognition ; such cases were formerly known as "blood-cysts of bone."

The Classification of New Growths

It is no easy task to frame a satisfactory classification of new growths. We are ignorant of their exact causation, and do not know whether it is in all cases the same. Their histogenesis is in some cases uncertain, and in many cases a matter of guesswork. The embryological origin of the cells from which they are believed to arise is, even at the present day, not in every case finally settled. Their clinical course affords no scientific ground for classification. The least unsatisfactory basis which can be taken for an orderly grouping of the new growths seems in the present state of knowledge to be the morphological, or rather histological one. Nevertheless, so far as histogenesis and embryology furnish us with reasonably certain data, these may very properly be taken into account in our scheme of classification.

A general consideration of the structure of tumours shows that they fall into three main groups, between which, however, transitional forms may be traced. These three groups are—(1) *Teratomas*, consisting of many tissues. (2) *Histioid and organoid tumours*, consisting of a single definite tissue, simple or complex. (3) Purely *cellular tumours*, forming no true tissue comparable to the normal adult type.

Teratomas.—These, as their name implies, were regarded by those who first observed them as marvels of portentous nature. Yet they are perhaps of more ready explanation than the simpler tumours, for in many cases they evidently represent another individual organism implanted, or accidentally developing, in the bearer. Their significance will be discussed later in the hypotheses which have been advanced to explain new growths. Here it will suffice to say that every transition can be traced between ordinary double monsters and cases in which one fœtus is imperfectly developed and partially included in one more perfectly developed. From such a condition it is an easy transition to instances in which the less-developed fœtus, forming an amorphous mass, may be regarded as a mere tumour included in, or appended to, its more highly developed brother, as in the well-known "epignathus"; in this two embryos are connected by their oral regions; one develops normally, while the other

merely forms a rudimentary lobulated mass, composed of various tissues miscellaneously arranged. With the invagination of the stomodæum to form the buccal cavity of the well-developed fœtus, the rudimentary one is drawn inwards, so that finally it is attached to the basis cranii, filling, and protruding from, the mouth of its fellow. All external semblance of a separate individual is here lost, and the mass is clearly to be regarded as a teratomatous tumour. Tumour-formations of the same sort occur in the sacro-coccygeal region, and are to be explained in an analogous way. Growths of similar histological structure, containing irregularly disposed masses of cartilage, nervous, hepatic, and other glandular structures, and indeed of almost all the bodily tissues, connected by indifferent or myxomatous tissue, are occasionally met with in various situations in the body —*e.g.* in the testis, ovary, or mediastinum, and are plainly of the nature of a second individual, the proper development of which has hopelessly miscarried, and which has become by some chance included in the body of another. The structure of such growths is often complicated by cyst-formation. From these the transition is easy to ovarian "dermoids," which frequently present not only epidermal structures, such as skin, hair, and teeth, but also bone, nervous tissue, and sometimes representative tissues from all three germinal layers. It is difficult to withhold from ovarian dermoids the rank of another "individual," *i.e.* the product of an ovum; and the same is probably true of the rarer testicular dermoids.

To all the above forms of tumour the term "teratoma" in its strict sense may be applied, or, if preferred, the term "embryoma" introduced by Wilms. Closely allied are tumours which, while not ranking as another individual, are yet traceable to developmental malformations, whereby portions of one or more tissues have become included in the wrong place. These are usually classed as teratoid or embryoid. Such are the "mixed tumours" met with in the testicle and kidney (adeno-sarcoma, rhabdomyo-sarcoma, chondro-carcinoma, etc.), and perhaps also the mixed parotid and palatine tumours. Amongst the simpler teratoid tumours are ordinary "inclusion dermoids," cholesteatomata of the meninges, aberrant hypernephromata, and even parovarian cysts and other cystic dilatations of embryonal remains. But from these simpler forms the transition to the group of "organoid" tumours is so easy that it is scarcely possible to draw a definite line.

Speaking generally, it may be said that the teratomata are in themselves innocent growths. Nevertheless they have a distinct tendency to form the starting-points of definitely malignant growths, sarcomatous, or more rarely carcinomatous.

Organoid and histioid tumours.—Virchow distinguished as "histioid" new growths consisting of a single tissue, and as "organoid" those composed of a fibrous stroma enclosing parenchymatous cells. This distinction cannot rigidly be maintained. It has been pointed out by Thoma (68) that every tumour has some sort of stroma, even if it consist only of blood-vessels. Virchow's histioid tumours are mostly those of the

connective-tissue type, and his organoid tumours those of epithelial derivation. Thoma groups them all together as "organoid," restricting the term to such as have a structure approaching to that of normal bodily tissues. Such a group includes all the benign tumours of comparatively simple texture; it is not, however, a sharply defined group, for on the one hand it is connected with the simpler teratoid tumours, and on the other it passes by insensible gradations into the group of cellular new growths. The relative proportion of cellular elements in a tumour is a numerical criterion which permits of no sharp line of demarcation, and it has been already pointed out that anaplasia and malignancy shade off insensibly into normal cell-structure and innocency.

Cellular tumours.—Nevertheless it is convenient to maintain Virchow's group of "cellular" tumours—growths consisting of no true tissue comparable to a normal one, but formed of cells, anaplastic in type, with or without a manifest fibrous stroma. These growths are essentially malignant.

A grouping of tumours, such as has been indicated above, is now commonly adopted, *e.g.* by Lubarsch, Powell White, and substantially by Thoma and others. Ziegler's primary classification presents some points of difference. He also divides new growths into three groups—(*a*) *the connective-tissue group*, including Virchow's histioid tumours and their anaplastic representatives—the sarcomas; (*b*) *epithelial tumours*, including Virchow's organoid tumours and their anaplastic representatives—the carcinomas. But he now includes in this group not only tumours of epiblastic and hypoblastic descent, but also those arising from the mesodermal epithelium, or endothelium, lining the great serous cavities, and from the epithelium of the kidney, suprarenal and sexual glands. (*c*) His third group contains the *teratomas and cysts.*

The first of these two classifications is seen to rest upon the purely morphological basis adopted by Virchow, while Ziegler's, though essentially morphological, takes some account of histogenesis and embryonic descent.

The Embryological Classification of New Growths.—Attempts have naturally been made to classify tumours according to the primary germinal layers from which their tissues are derived. It might well be supposed that such a grouping would prove the most natural and scientific, yet the older attempts at an embryological classification were far from satisfactory. An endeavour was made to identify the epithelial group of tumours with the epiblast and hypoblast, and the connective-tissue series with the mesoblast. This grouping, still found in some text-books, will not bear criticism, for it involves us in numerous difficulties, separating growths which are nearly allied, and placing together those which are widely different. The alveolar structure of certain endotheliomas places them very close to the carcinomas. The carcinomas arising in the kidney, suprarenal, ovary, testis, and body of the uterus seem unquestionably of mesoblastic descent, while a cerebral glioma, though a typical connective-tissue tumour, is, according to Golgi, His, and other

more recent embryologists, no less certainly epiblastic. Hansemann has inveighed against the tendency to regard epithelium as a special kind of tissue, considering such a view a great source of confusion. He insists that the "epithelial" character consists in the juxtaposition of cells lining a surface, and not in the morphological character of the cells or their germinal descent.

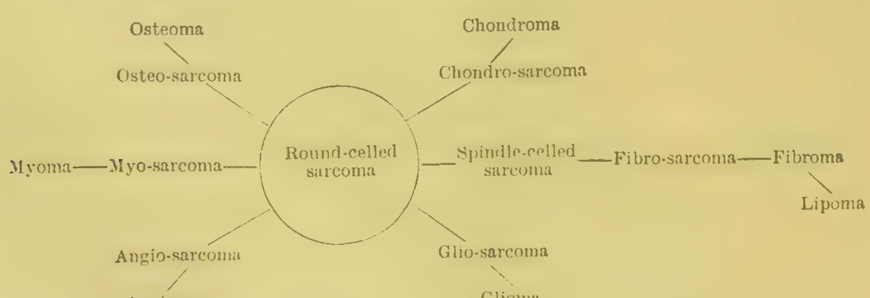
Professor Adami (1), aided by well-known embryologists, such as Minot, has propounded a classification of tumours based on the more modern developments of embryology. The basis of his grouping, which seems in many respects the most satisfactory yet advanced, rests on the following facts. (1) The segmenting ovum separates into epiblast and hypoblast; from the latter arises the primitive mesoblast. The hypoblast further originates the notochord, and then forms the epithelial tissues of the alimentary canal, and of its associated glands, as has always been recognised. The epiblast gives off the neuroblast, and then originates the epiderm with its appendages and invaginations as generally admitted. The mesoblast forms the origin of two tissue-groups—the mesothelium and mesenchyme. The mesothelium lines the serous cavities, and gives rise to the adrenals and urogenital system; later the voluntary muscles and heart muscle seem to arise from it. The mesenchyme is the parent of all the various connective tissues, of the unstriped muscular system, of the spleen and blood-vessels. (2) The tissues of the body fall into two main groups—those which coat its surfaces, and those which form the supporting framework. These Professor Adami terms, respectively, "lepidic,"[1] or lining-membrane tissues, and "hylic,"[1] or pulp-tissues. Examples of each of these can be traced to all three primary germinal layers. He points out that the natural grouping of tumours does not depend on their origin in epiblast, hypoblast, or mesoblast, but on whether they arise in "lining-membrane tissues" or in "pulp-tissues." Such a grouping is a natural one, and is identical with that adopted by Ziegler. Lining membranes cover surfaces or line spaces; they originate glands, which are supported by a framework of pulp-tissues (stroma); their cells form groups into which blood-vessels do not penetrate; there is no stroma between the individual cells, only between cell-groups (alveolar structure). The pulp-tissues, on the contrary, have an intercellular ground substance, and blood-vessels run amongst their cells. These, it may be noted, are the very points upon which we are accustomed to rely in distinguishing between carcinoma and sarcoma.

Professor Adami goes further than Ziegler in his subdivisions, and has proposed a terminology which, if a little cumbrous, is certainly reasonable, and may perhaps gain acceptance. He terms the growths arising in "lining-membrane" tissues "*Lepidomata*," subdividing them, according to their germinal origin, into epilepidomata, mesolepidomata, and hypolepidomata. The growths arising in "pulp-tissues" he terms

[1] From the Greek λεπίς, a rind, husk or scale, and ὕλη, a wood, or, secondarily, raw material or pulp.

"*Hylomata*," similarly subdividing them into epihylomata, mesohylomata, and hypohylomata. Whether or not these precise terms gain current usage, the grouping seems a more natural one than most of those which have been suggested, and is an ingenious combination of the strictly embryological and the histogenetic principles of classification. Each term implies not only the general histological character of the tumour, but also its origin from the germinal layers. Even the endotheliomas, the classification of which has given rise to so much discussion, fall naturally into position as "mesolepidomata."

Terminology.—The individual terms employed to designate the different forms of new growth are based on their histological structure—the suffix "oma" being added. Such terms as fibroma, chondroma, osteoma, lipoma, and so forth, explain themselves. Where two or more tissues are intermixed in a tumour, such terms as "fibro-lipoma," "osteo-chondroma," and the like, may be employed. A growth of pure mucoid tissue is a "myxoma"; where a fibrous or cartilaginous growth has undergone partial mucoid degeneration, we speak of a "myxo-fibroma" or "myxo-chondroma." The anaplastic forms of the "pulp-tissue" groups are termed "sarcoma," and the degree of anaplasia is usually implied in a prefix denoting the form of the cells. The round-celled sarcoma exhibits the highest degree of anaplasia; next in order comes the oval-celled, and then the spindle-celled sarcoma, while for those of mixed type the designation "mixed-celled" sarcoma has to be used. The transitions between malignant and innocent forms in this group are customarily named fibro-sarcoma, chondro-sarcoma, osteo-sarcoma, angio-sarcoma, etc., according to the nature of their tissue-elements. Mr. Butlin prefers the terms "fibrifying," "chondrifying" sarcoma, etc., as indicating that the fibrous and cartilaginous elements are developed from the sarcoma-cells themselves. In fact, inasmuch as the origin of all the different adult forms of connective tissue can be traced back in the earlier embryonic stages to a simple round cell, one may readily reduce the whole series of tumours of this group to diagrammatic form by representing them as diverging from the simple round-celled type; thus:—



In such a scheme, designed only to represent the commoner types, the extreme term of each radius is an innocent growth; the intermediate terms represent varying degrees of malignancy, culminating in the central

type from which we may conceive all to have diverged—the most anaplastic and malignant of them all.

The terminology of the epithelial and endothelial series of new growths is based on similar lines. Of the simple forms we have the innocent warts or "papillomata," and the glandular tumours or "adenomata." The anaplastic types are included under the general term "carcinoma," with the prefixes "squamous-celled," "columnar-celled," "spheroidal-celled," according to the type of epithelium concerned. Whatever the primitive form of epithelium, such growths tend, with increasing anaplasia, to lapse into the indifferent or spheroidal-celled type. The term "epithelioma," which is in use in this country as a synonym for squamous-celled carcinoma, is, on the Continent, and especially in France, used indiscriminately for any sort of epithelial new growth, even an innocent one, and it is therefore advisable to discard it.

The *endotheliomas* form a group at present much under discussion. With the discovery that some cancer-like growths may originate from endothelium, there has arisen a tendency to baptize any puzzling cellular tumour an endothelioma, often with little enough justification. The delimitation of the endothelial group of tumours is at present far from clear, and the matter is not simplified by the fact that growths of undoubted endothelial origin present very various histological features. Two main groups are certainly recognisable—the "lymph-endotheliomas" and the "hæm-endotheliomas," arising respectively from the endothelium of lymph-spaces and blood-vessels, while in a third group, the "peritheliomas," the growth appears to originate in the perivascular lymphatics. Of these various groups some have evident relations with the carcinomas, others with the sarcomas, and in particular with the angio-sarcomas, with which, indeed, they are largely identical. It is probable, but by no means certain, that many, perhaps all, of the tumours formerly classed as "alveolar sarcoma" will be shown to be of endothelial origin. As a whole, the endotheliomas seem of more benign disposition than the carcinomas and sarcomas. Many of them are quite innocent, and pass into the lymphangiomas and nævi by insensible gradations, being, as it were, but the more solid forms of these. The endotheliomas of the meninges are habitually, but not invariably, innocent, and the same is true of the mixed parotid and mixed palatine tumours. The endothelial nature of the latter groups, supported by Volkmann and many subsequent writers, has been vigorously contested by Hinsberg and others, and must be taken as a doctrine rather than as proved; the simulation of glandular tissue is occasionally very striking. On the other hand, endotheliomas are met with which behave in all respects as malignant tumours, though often of somewhat slow course.

Cystic Tumours.—Many tumours are essentially cystic in nature—the cysts being an integral part of the structure of the growth, not secondary or adventitious. To such the term "cystoma" has been applied. Where, as in the case of the multilocular ovarian cysts, the tumour is composed merely of a congeries of cavities with a simple epithelial lining, the term

cystoma expresses all that is needed. But cystic tumours are often complicated by the development of intracystic growths. These may be protrusions of the stroma into the cavity, covered only by an epithelium like that which lines it elsewhere. There is a common form of fibro-adenoma of the breast in which such protrusions of the stroma into the gland-spaces reach a high degree of complexity; it is the variety known as "fibroma intracanaliculare"; Brodie called it "serocystic disease." But more commonly the intracystic growths are due to epithelial proliferation, with only a scanty supporting stroma; these, too, may attain great complexity of structure, and may have the appearance of glandular tissue. In such cases, where the intracystic growths are innocent in type, the term "adeno-cystoma," or "cystadenoma," is employed for the tumour (= papilliferous cyst or proliferous cyst of former writers). Adeno-cystomas are common in the ovary, and not rare in the kidney and breast; they may, indeed, occur in many organs. Finally, epithelial intracystic growths may be truly cancerous in nature; their epithelium may exhibit anaplasia, and they may infiltrate beyond the bounds of the cysts themselves, and give rise to metastases. The term "villous cancer" is sometimes used for this variety. Such cystic carcinomas or carcino-cystomas are especially common in the ovary; "duct-cancer" of the breast is another example.

It may be useful to append a detailed classification of new growths. Such an attempt, in the present state of our knowledge, must of necessity be imperfect and tentative; some cross-classification is inevitable, and the writer does not expect to escape criticism, for it would be difficult to find two pathologists in perfect agreement as to the principles upon which such a grouping should be carried out, or even as to the detailed nature of many of the growths included. The following table does not pretend to absolute completeness:—

I. **Tumours derived from the Supporting or Connective Tissues** (and from their more specialised allies—vascular and muscular tissues).

- A. Tissue of adult type.
  - (*a*) Of mesoblastic (mesenchymatous) origin.
    1. Fibrous tissue. *Fibroma* (lamellar or fascicular, hard or soft). (*False neuroma.*) Cheloid.
       with partial or complete mucoid degeneration. *Myxo-fibroma* and *Myxoma.*
    2. Fatty tissue. *Lipoma.* Variety *Diffuse Lipoma.*
       combined with fibrous tissue. *Fibro-lipoma.*
       combined with nævoid tissue. *Angio-lipoma.*
       with mucoid degeneration. *Myxo-lipoma.*
    3. Cartilage. *Chondroma.* Enchondroma, Ecchondrosis.
       partially ossified. *Osteo-chondroma.*
       with mucoid degeneration. *Myxo-chondroma.*
    4. Bone. *Osteoma.* Cancellous and compact exostoses.
       from hard structures of teeth. *Odontoma.* Dental exostosis.

5. Muscle. *Myoma.*
   Unstriped. *Leiomyoma.*
   combined with fibrous tissue. *Fibro-myoma.*
   Striped. *Rhabdomyoma* (not occurring as an independent tumour).
6. Vascular tissue. *Angioma* (with transitions to some forms of endothelioma).
   α. composed of blood-vessels. *Hæmangioma.* Nævus.
   capillary : birth-mark, capillary nævus, angioma simplex hypertrophicum.
   venous : cavernous nævus.
   arterial : racemose aneurysm.
   β. composed of lymphatic vessels. *Lymphangioma.*
   with cystic dilatation. Cystic hygroma.
7. Lymphoid tissue. *Lymphoma.*

(*b*) Of epiblastic origin.

8. Neuroglia. *Glioma.*

(*c*) Of hypoblastic origin.

9. Notochord. *Chordoma.*

B. Tissue of anaplastic type (partially or wholly). *Sarcoma.*

(*a*) Lesser degrees of anaplasia.

10. Bone-marrow type. *Myeloma.* Myeloid sarcoma. Multiple myeloma.
11. Transitional forms to innocent growths.
    Fibro-sarcoma.
    Chondro-sarcoma.
    Osteo-sarcoma.
    Myo-sarcoma.
    Angio-sarcoma.
    Hæm-angio-sarcoma } endothelioma in
    Lymph-angio-sarcoma } part.
    Glio-sarcoma.

(*b*) Higher degrees of anaplasia.

α. Wholly cellular, with inconspicuous stroma.

12. *Round* and *oval-celled sarcoma.* (? Chloroma.)
    Spindle-celled sarcoma.
    Mixed-celled or *irregular-celled sarcoma.* Giant-celled sarcoma (not myeloid).
    β. with diffuse fibrillar stroma. *Lympho-sarcoma.*
    γ. with conspicuous stroma. *Alveolar sarcoma* (endothelioma in part).
    δ. derived from pigmented tissues. *Melanoma.* Melanotic sarcoma.
    ε. with mucoid degeneration. *Myxo-sarcoma.*

II. **Tumours derived from Nervous Tissue.** *Neuroma.*

13. Composed of nerve-fibres (medullated or non-medullated). *Neuroma verum.* *Plexiform neuroma.*
    Containing ganglion-cells. *Neuroma ganglionare.*

III. **Tumours derived from Endothelium.** *Endothelioma.*
of mesothelial origin.

14. (*a*) From lymphatic endothelium. *Lymph-endothelioma.*
α. from serous surfaces. *Endothelioma carcinomatosum.*
β. from meninges.[1] *Endothelioma vel Fibro-endothelioma meningeale.*
with focal calcification. *Psammoma.*
γ. from lymphatics and tissue-spaces.
innocent. *Lymph-angioma hypertrophicum. Verruca carnea.*
anaplastic. *Lymph-angio-sarcoma.* Alveolar sarcoma.
δ. from perivascular lymph-spaces. *Perithelioma.*
? Glioma retinæ.
ε. with hyaline degeneration. *Cylindroma.*
combined with mucoid tissue and cartilage. *Myxo-chondro-endothelioma.* Mixed parotid and palatine tumours.
(*b*) from hæmal endothelium. *Hæm-endothelioma.*
innocent. *Hæm-angioma hypertrophicum.* Hypertrophic nævus.
anaplastic. *Haem-angio-sarcoma.*

IV. **Tumours derived from Epithelium** (whether of epiblastic, mesoblastic, or hypoblastic descent).

A. Tissue of adult type.
15. Squamous epithelium. *Papilloma.*
Transitional epithelium. *Papilloma vesicæ.*
16. Columnar, cubical, and spheroidal epithelium.
(*a*) Solid glandular tumours. *Adenoma* (alveolar or tubular).
with abundant fibrous stroma. *Fibro-adenoma.*
with mucoid stroma. *Adeno-myxoma.*
with anaplastic (sarcomatous) stroma. *Adeno-sarcoma.*
17.
(*b*) Cystic glandular tumours. *Cystoma.*
with intracystic growths
of stroma. *Fibroma intracanaliculare.*
of epithelium. *Cystadenoma. Adenocystoma papilliferum.*

B. Tissue of anaplastic type. *Carcinoma.*
18. (*a*) Derived from fœtal (chorionic) epithelium. *Syncytioma malignum.* Deciduoma. Chorion-epithelioma.
19. (*b*) Derived from adult tissues.
α. Squamous epithelium. *Squamous-celled carcinoma.*
from the appendages of the epidermis. *Rodent ulcer.*
β. Columnar epithelium. *Columnar-celled carcinoma.*
γ. Spheroidal epithelium. *Spheroidal-celled carcinoma.*
Carcinoma simplex.
with dense fibrous stroma. *Scirrhus.*

[1] It is possible that some of the meningeal endotheliomas are of hæmal origin.

δ. Cystic tumours with anaplastic intracystic growths. *Cysto-carcinoma papilliferum.*

ε. with mucoid degeneration
of epithelial cells. *Carcinoma colloides.*
of stroma. *Carcinoma myxomatodes.*

V. **Tumours derived from several different Tissues.** *Teratoma.*

20. A. Representing another individual. *Teratoma verum. Embryoma.*

B. Representing misplaced portions of the bearer. *Teratoid and mixed tumours.* Sequestration-dermoids, cholesteatoma, etc.

Hypotheses as to the Nature and Causation of New Growths

Conjecture has at all times been rife as to the essential nature and pathogenesis of tumours, and a large amount of investigation and experiment has been devoted to the subject. The matter is one not merely of speculative interest, but has evident practical bearings, for it is plain that a knowledge of the causation of new growths is an essential preliminary to rational treatment. Till this is attained we must remain dependent upon the knife.

In the majority of cases tumours appear to arise spontaneously, though in some instances an exciting cause seems to be present. Growths are specially apt to arise in tissues which are in an abnormal condition—abnormal either from perverted situation or from the effects of injury or chronic irritation. *Chronic irritation* is too frequently associated with tumour-formation to admit of any doubt as to their relation. Irritative hyperplasia of tissues is a well-recognised condition, and from this to the development of a definite new growth is a step which may at first sight seem an easy one. Yet it is a transition not readily explained on logical grounds, since the autonomy of the resulting tumour must be accounted for. Instances of tumours resulting from chronic irritation can be adduced in numbers. The museum of St. Bartholomew's Hospital affords specimens of cheloid, of innocent fibroma, of sarcoma, and of squamous-celled carcinoma arising in the scars of chronic ulcers. The irritation of a jagged tooth is recognised as a precursor of some cancers of the tongue, and that produced by a pipe of many similar growths of the lip. Chimney-sweeps' cancer of the scrotum is probably determined by the accumulation of soot in the folds of that region. Primary carcinoma not uncommonly arises in an already cirrhotic liver.

It seems equally clear that *mechanical injury* is sometimes a direct antecedent of new growths. Yet such injuries are so exceedingly common that it is no matter for surprise that careful inquiry should often elicit a history of the kind. Few of us escape occasional blows, and it is therefore needful to sift very carefully the evidence which seems to connect a tumour with a traumatic cause. If too much reliance be

placed on the statements of the patient, there is considerable danger of overestimating the part played by injury in this connexion. It has been justly pointed out by Thiem that injury should only be recognised as a causal factor when the tumour arises at the very site of the original injury, and when a continuous series of local phenomena intervenes between the injury and the appearance of the growth. An analysis of 920 cases at Strasburg led Machol to reduce the percentage in which trauma really played a part in the causation of new growths to 2·06, though, according to the patients' histories, it would have been as high as 11·73 per cent. Similarly, Lengnick in 579 cases could only convince himself of a traumatic origin in 2·07 per cent. Other observers have recorded a much larger percentage than this. It is noteworthy that Machol found sarcoma much more commonly due to injury than carcinoma—roughly as 9 to 1—and this seems in accord with general experience. I have had the opportunity of examining one case in which malignant disease appeared directly to follow upon a surgical operation. The patient was a man, aged 62 years, who suffered from a urethral stricture due to gonorrhœa. In connexion with this an abscess formed in the perineum and burst, leaving a permanent fistula. He was admitted to St. Bartholomew's Hospital, where Mr. Butlin performed an external urethrotomy. No suspicion of new growth existed at the time of the operation, but the perineal wound never closed, began to fungate, and three months after the operation was found to be the seat of a squamous-celled carcinoma, which both histologically and clinically was of a peculiarly malignant character. The mechanisms by which chronic irritation and injuries have been conjectured to set up tumour-formation are (1) by the displacement of cells from their natural connexions, (2) by the setting up of chronic inflammatory changes and the over-nutrition of the part by the temporarily increased blood-supply, and (3) by lowering tissue-resistance either against the normal cell-growth of the local tissues or against hypothetical parasites. These various views will be considered in more detail a little later.

There are certain other indirect or predisposing causes which have at different times been discussed in relation with the origin of new growths. The only ones which need be considered in any detail are heredity and endemicity.

In the popular mind *heredity* plays a large part in the incidence of tumours, nor can it be denied that certain families show a marked disposition. One of the most striking cases is that recorded by Broca. A woman died in 1788 of cancer of the breast: four of her daughters died of cancer, and in the succeeding generations, ten grandchildren and one great-grandchild of the same complaint. It is even more striking when this family disposition shows itself in a single organ: according to Vierordt, Napoleon I. and two of his sisters suffered from carcinoma of the stomach, as their father had done before them. Many similar cases have been recorded, and may well make us hesitate before denying that there is some truth in the popular view as to hereditary

influence. Nevertheless there is good reason for believing that this factor has been overestimated. Tumours are very common, and in one form or another a large percentage of the population suffers. Leaving innocent tumours out of the question, it is stated by Dr. Newsholme that, on the basis of the figures for 1896, 1 in every 14 males and 1 in every 9 females, who reach the age of 35, die ultimately of "cancer," and the number is alleged to be an increasing one. In these circumstances it is plain that, merely on mathematical probabilities, any patient should, more often than not, be able to point to a relative with a tumour of some kind. The only statistics which would be of serious value are precisely those which are the most lacking—those showing the occurrence of similar growths in the same organ in members of one family. In the case of a man with a round-celled sarcoma of the testis, we can hardly attach much importance, from the point of view of heredity, to the fact that his mother had a scirrhus of the breast or his great-aunt a multilocular ovarian cyst. At the most these facts only justify the conclusion that his family showed a general disposition of the tissues to tumour-formation, which is a very different thing from the inheritance of cancer. This, in short, is the view now generally held on this point.

Much has also been made of the *endemicity* of cancer. In an extensive work, published in 1875, Haviland plotted out in a map the cancer mortality amongst females in the 623 registration districts of England and Wales. His general conclusion was that the cancer mortality is lowest in those districts formed of hard and elevated rocks, or of absorbent rock such as chalk, and that it is highest along the course of rivers which seasonally flood their banks, and on flat alluvial soils generally. In such situations the cancer mortality may be more than three times as great as in elevated rocky districts. The facts are certainly striking, but it is not clear that the interpretation holds good for all countries: it is asserted that in Norway and also in Mexico the facts are quite different. Instances have also been brought forward, for example by Dr. T. Law Webb, in which cases of cancer have repeatedly occurred in single houses or in small groups of houses, which have hence been regarded as foci of infection. Such instances are not very numerous, and they form such an infinitesimal part of the total cancer mortality that it would be rash to pay undue attention to them in considering the causation of the disease.

No *age period* is exempt from new growths, but, apart from the teratomas and other congenital tumours, they appear gradually to increase in frequency with advancing years. Carcinoma is well recognised as essentially a disease of later life, while sarcoma occurs more impartially at all ages. The alleged increase in cancer mortality, mainly attributable to more accurate certification of death, may perhaps be also in some part due to the lowering of the death-rate—*i.e.* to the higher average age at death. The lives of the young saved by improved sanitation from zymotic and similar diseases, may perhaps help to swell the cancer mortality of later life. (*Vide* p. 55.)

It has been suggested that the more artificial the conditions under which a race lives, the more liable is it to new growths. The frequency of tumours in the more highly civilised races and in domesticated animals has been put forward in support of this view. Without denying the possibility of such an etiological factor, it must be pointed out that our knowledge of the relative frequency of tumours amongst savage races and in wild animals is of so slender a description that we have no sufficient data for forming a valid opinion on the subject.

Passing from these general considerations, the more precise hypotheses as to the causation of new growths fall into two groups—those which seek to explain them by some cause acting from without, and those which trace them to more intimate causes acting within the body itself.

Of the *extrinsic* conceptions of tumour-causation, only one need be considered in any detail—that which traces them to infection by a parasite. The action of chronic irritation and trauma, though in a sense extrinsic, may be more properly conceived of as liberating one or another of the intrinsic causes to be discussed later.

The Parasitic Hypothesis of New Growths.—Even an innocent tumour is, almost by definition, a structure parasitic upon the body which bears it. Much more obviously is this the case with malignant growths, which exhibit the phenomena of parasitism in a high degree; the way in which they destroy adjacent tissues and give rise to metastases—the facts of auto-inoculation and transplantation—stamp them as eminently parasitic in character. It is therefore in no way surprising that they should have been assumed to owe this character to the presence of an infecting micro-organism.

Much has been made of an analogy between a malignant growth and such a chronic infective process as tuberculosis; it has been argued that as the latter is known to be an infection, so in all probability is the former. An examination of the analogy shows that it is essentially a misleading one. When a primary tuberculous focus gives rise to secondary tubercles elsewhere, it does so by the dissemination of the tubercle bacillus, not of the constituent cells of the tubercle: the secondary "tumours" which arise are built up locally by the proliferation of the tissues where the bacillus chances to lodge. But when a primary focus of malignant disease gives rise to metastatic growths, it does so by the transference of its own cells, and the secondary foci are developed by the local growth of the transported cells, not by the proliferation of the indigenous tissue-elements; these at the most are utilised as an unessential stroma. If the development of the secondary growth were due to the dissemination of a parasite, we should expect this parasite to excite a malignant transformation of the local tissue-elements, which is precisely what does not occur. The secondary growths breed true and maintain the essential histological characters of the primary tumour.

This analogy must therefore be dismissed. The parasitic origin of malignant growths must stand or fall on the positive evidence which can be produced in its favour.

The last decade of the nineteenth century stands out as a period in which the search for "cancer-parasites" was keen and unremitting. The germ-theory of disease had been established on a firm basis, and to many there seemed good reason for believing that malignant growths might be thus explained. Earlier attempts to demonstrate bacteria as the exciting cause of cancer had already proved without sufficient foundation, but in 1889 "coccidia" were described by Malassez, and similar structures by Thoma (69). It was known that coccidia caused papillomatous growths in the bile-ducts of the rabbit, just as the ova of Bilharzia cause similar growths in the human bladder and rectum. Soon afterwards Darier, and later Wickham, described the same appearances in Paget's disease of the nipple. Dr. Russell in 1890 brought forward his "fuchsin bodies" in cancer, and in 1892 papers appeared by Soudakewitch and by Drs. Ruffer and Walker. Metchnikoff lent the weight of his support to the view that the bodies described and figured by these writers were truly parasitic protozoa. Since that time many other observers have followed on the same lines; it must suffice to mention the names of Plimmer (42) in this country and Gaylord in America. The life-history of the parasite was reconstructed from the histological appearances, and it must be confessed that the coloured plates which were published left little to be desired. Towards the end of the decade in question the vogue changed somewhat; the parasite was transferred by Sanfelice, Roncali, and other Italian workers from the Protozoa to the Blastomycetes. These observers did what the upholders of the coccidial hypothesis had failed to do. They actually cultivated pathogenetic yeasts from cancers, and claimed to reproduce the disease with their cultures. Mr. Plimmer (43) has obtained similar results in England.

There is thus some diversity in the appearances described; but an impartial study of the facts can leave no doubt upon the mind that if the growing edge of a cancer be properly fixed and stained with suitable dyes, rounded cell-inclusions are commonly demonstrable, which might bear the interpretation of parasites. It is to be regretted that many of those who wrote on the subject have described as parasites cell-inclusions —such, for example, as ingested leucocytes—which were evidently nothing of the sort. Russell's fuchsin bodies seem clearly to be local areas of hyaline degeneration in the cells (cf. p. 572). We may indeed go further than this and assert that the minute cytological studies of recent years are capable of explaining a large part of the appearances which have been taken for parasites. The peculiar mitoses of malignant growths yield irregular chromatin residua, and the degenerations which these may undergo lead to very curious appearances; the nucleolus, too, may stain in unusual ways in cancer-cells. Mr. D'Arcy Power described a number of cell-changes in tissues artificially irritated, some of them not dissimilar to the appearances seen in cancer. There have never been wanting those who have persistently discredited the parasitic hypothesis, and amongst these may be named such well-known pathologists as Hansemann and Lubarsch

—indeed the hypothesis has never enjoyed such vogue in Germany as in France and Italy.

But even if we concede the parasitic nature of the bodies described in cancer by the more trustworthy observers, we are still a long way from the proof that such bodies have any causal relation with the disease. That pathogenetic yeasts have again and again been grown from cancers is unquestionable: it is when the attempt is made to reproduce the disease with such cultures that the case breaks down. In the opinion of most of those who have examined the preparations from the alleged growths thus produced, these are not true new growths, but inflammatory formations, perhaps of the nature of infective granulomata. It is indeed well known that certain yeasts can give rise to conditions of the kind. Perhaps the most definite new growths which have been produced are those of Nils Sjöbring (62), who maintained that he cultivated rhizopods from malignant growths in a gelatin medium containing sugar and a potash soap prepared from human fat. With such cultures he gave rise, in mice, to tumours which he showed at a meeting of the German Pathological Society at Aachen in 1901 (63); in the opinion of Lubarsch one at least of the tumours was a true adeno-carcinoma, but the "rhizopods" in his cultures were almost unanimously pronounced to be degenerate carcinoma-cells.

It must be confessed that after fifteen years of painstaking labour the positive evidence in favour of the parasitic origin of cancer has failed to carry conviction to most pathologists. And although it is still necessary to keep an open mind on the subject, it is far from clear that such a conception would not introduce more difficulties than it explained. It is obvious that carcinoma and sarcoma must stand or fall together, and it is equally obvious, though too often overlooked, that no hard-and-fast line separates malignant from innocent tumours, and that it is logically necessary to include the latter in the parasitic hypothesis if it be shown true for cancer. If we survey, for example, the cystic tumours of the ovary we find every conceivable transition from the simple cyst, through the multilocular cyst, to cysts having intracystic growths which consist now of fibrous, now of epithelial tissue; and from innocent, adenomatous intracystic growths we pass, still by insensible gradations, to cancerous ones which give rise to metastatic growths in the peritoneum, liver, and elsewhere. It seems impossible to draw a line, and to say that the cancerous ones own a parasitic origin, the rest not: if one is parasitic, all must be so. The development of a suprarenal "rest" in the kidney into a tumour which is in one case an innocent adenoma, in another a malignant carcinoma, is an argument in the same direction. Indeed, all the facts, and they are not a few, which support the view of Cohnheim to be mentioned below, are obstacles in the way of the parasitic hypothesis. The persistence of histological character in metastatic growths is a circumstance very difficult to surmount: it seems certain that here, as in transplantation experiments, the new tumour is a lineal descendant of the cells of the primary growth, and not due to any transference of a parasite

other than the malignant cell itself. Nor do the difficulties end even at this point. It has been mentioned above that malignant growths are inoculable only within the limits of the same species. This would seem logically to involve, for each species of animal liable to cancer, a private and particular variety of cancer-parasite, incapable of producing the disease in any other sort of animal. Such a view is incredible in face of the close resemblances between these growths in different vertebrates.

Finally, it may be urged that the parasitic hypothesis of cancer is superfluous. The eminently parasitic characters of malignant growths are quite well explained on the assumption that the cancer-cell or sarcoma-cell is itself the parasite. We see these cells, as they infiltrate the normal tissues adjacent, or as they are disseminated in distant parts, behaving in all respects as foreign or parasitic organisms. The essence of all new growths, whether malignant or innocent, is an autonomy which is practically equivalent to parasitism. What need then, as Professor Adami (2) has justly argued in the case of syncytioma malignum, to postulate a parasite as the cause of parasitism? Opinion has indeed been gradually coming round to the view that the origin of new growths in general, and of malignant ones in particular, is to be sought in some intrinsic cause which has wrought a change in the biological properties of the cell or cells from which they have arisen, rather than in any invasion by an extrinsic parasite for which no adequate proof has yet been forthcoming.

Intrinsic Conceptions of New Growths.—The problem, as has been urged, is to explain the autonomy of tumours. It has to be shown why a certain cell-group behaves towards the rest of the body as a foreign organism, governed by its own laws.

In the true teratomas the explanation lies more or less on the surface. The tumour is a foreign organism—another individual—the product of another ovum, or at least of an early division of the same ovum. There is no reason why it should subordinate itself in any way to the needs of the host in which it has had the misfortune to be included. The true teratomas appear soon to reach the limits of their growth; they are habitually innocent tumours, though it is by no means rare for certain of their contained cell-groups to become later, and as it seems secondarily, endowed with the more aggressive independence which we term malignancy.

There is one example of a typically malignant growth, viz. syncytioma malignum (chorion-epithelioma), in which a somewhat similar explanation holds. There is now a fair agreement amongst pathologists that this growth is derived from the fœtal chorionic epithelium. Its common association with an antecedent pregnancy—often a pregnancy which has gone wrong—the striking histological similarity with the syncytial tissue of the chorion, and the known aggressive properties of the trophoblast in the early formation of the placenta all point strongly in this direction. Here, then, is an eminently malignant growth, the autonomy of which is traceable to the fact that it is a part of another organism, and indeed a part

which under physiological conditions is known to be of parasitic and invading tendencies.

Mr. Shattock, who accepts the view that ovarian and testicular dermoids are of altogether different nature from the sequestration dermoids of the trunk, suggests that they arise from the fertilising of primordial ova in the embryo by spermatozoa which remained over after the fertilisation of the egg. In the case of testicular dermoids this would imply the presence of primordial ova in the testis—hermaphrodite conditions being not unknown in man. He terms this hypothesis "epigenesis," using the word in a different sense from that in which it has usually been employed in embryology. The phenomenon of parthenogenesis in lower animals, in which the ovum is fertilised by one of the polar bodies, renders such a hypothesis hardly necessary.

With the exception of the teratomas and allied tumours, and of syncytioma malignum, we have no positive and direct evidence, at the present time, that new growths in general are equivalent to or derived from other individuals. Such a view may indeed be held, but on indirect and abstract grounds (see later under "Biological Suggestions"). So far as the histogenesis of the majority of tumours is known, it points to their origin from the ordinary tissues of the body in which they develop. Some explanation, then, is required of their assumption of autonomy, and various views have been put forward. Cohnheim sought a developmental explanation in his well-known hypothesis of embryonic residua. Ribbert (46) invokes a pathological disturbance of tissue-relations, whereby a diminished resistance is produced against the inherent powers of growth possessed by every cell. There is much to be said in favour of both these hypotheses, and they must be mentioned in more detail.

Hypothesis of Embryonic Residua.—The credit of this view, as Monti justly points out, should properly be assigned to Durante. Nevertheless it goes by the name of Cohnheim's theory, since it is to the brilliancy of his advocacy that its acceptance has been chiefly due. It is shortly as follows. If, in the course of individual development, part of a germinal area, or of a cell-group destined for a particular organ or tissue, become by misadventure displaced and included in an unusual position, such aberrant cells, detached from their natural surroundings, may later take on abnormal growth and form the starting-point of a tumour. If, again, in the building up of a given tissue the whole of the embryonic cells provided for the purpose be not utilised, the redundant cells might remain dormant amongst their fellows, and possibly wake up in later life still in full possession of their inherent powers of growth and development. On such lines Cohnheim sought to explain the origin of every kind of tumour.

It is certain that many teratoid tumours originate in miscarriages of the normal course of development. The growths arising in connexion with the branchial clefts, the dentigerous cysts and multilocular cystic tumours of the jaw are cases in point. There is positive evidence that cell-groups do go astray in development—witness the suprarenal "rests"

so often seen in the kidney and sometimes found in the liver, in the broad ligament or spermatic cord. Adenomatous growths having the macroscopic and microscopic characters of suprarenal tissue, and also undoubtedly malignant tumours of peculiar structure which in all respects resemble those starting primarily in the suprarenal gland itself, arise primarily in the adult kidney, and therefore justify the conclusion that they are derived from suprarenal "rests" embedded in the kidney. The situation of some multiple exostoses and chondromas near the epiphyses of the long bones is such as to suggest their origin in misplaced rudiments of cartilage.

There is hence sufficient ground for the belief that some tumours do originate in areas of tissue which have gone astray in the course of development. But it is a long way from this to Cohnheim's assumption that all tumours have such a source. There is little evidence of such a universal distribution of embryonic inclusions or of dormant cells as his hypothesis demands. Even if this were assumed, the conception would not account for the revivifying of such dormant cell-groups, perhaps fifty years or more after their sequestration. But although something more is required to explain this, Cohnheim's hypothesis has the merit of explaining the seat of origin and histological characters of certain tumours; in a sense far more restricted than that in which he put it forward, it may be accepted as a permanent contribution to our knowledge of the nature and causation of new growths.

In this connexion may be mentioned the observations of Dr. Beard on the going astray of the primary germ-cells themselves in the early stages of development in elasmobranch fishes. The number of primary germ-cells is always some multiple of two. The embryo, in his opinion, arises from one of these, and the remainder should pass to be included in the sexual gland of this embryo, to hand on the germ-plasm to future generations. Now in Pristiurus Dr. Beard found that of the 127 primary germ-cells which ought to have reached the germinal ridge, only 90 to 100 could ever be demonstrated there. In the ray he states that 25 to 30 per cent of these cells go astray, and that he has demonstrated these vagrant germ-cells in various situations; most of them doubtless undergo degeneration, but he finds them especially in the stomach, rectum, and skin, *i.e.* in places which in man are common seats of cancer. Dr. Beard is a somewhat vehement exponent of a biological doctrine of new growths which will be mentioned later; but the facts just mentioned are of interest in connexion with the Cohnheim hypothesis.

Ribbert's hypothesis suggests the incidental detachment of adult cells from their physiological connexions as the determining cause of new growths, and of malignant tumours in particular. It is not easy to see how mere physiological detachment should endow cells with new powers of independent growth and activity. It is therefore necessary to postulate for every cell indefinite powers of multiplication, kept in check under natural conditions. Ribbert adopts the views of Thiersch and of Boll,

that the essential cause of new growths is a diminution in the natural resistance of the surrounding tissues. He conceives that, when development is completed, the various tissues and their constituent cells exercise a mutual restraint upon further multiplication; he uses the term "*tissue tension*" to express this idea. The cells would grow and multiply if they could, but they are prevented from doing so by the competition of their fellows. Should a cell or a group of cells become pathologically isolated from its neighbours this restraint is removed. Such isolation may be due to trauma, or, more often, to chronic inflammation. When, for example, a cancer arises from an epithelial surface, Ribbert would trace it not so much to an active invasion of the deeper tissues, due to a primary change in the properties of the epithelial cells, as to an ingrowth of the deeper tissues into the epithelium, whereby a group of epithelial cells becomes isolated and freed from the restraints imposed by its natural fellows. Thus liberated it is able to follow its own inherent powers of multiplication: the essential point is the diminution of resistance. Dr. Powell White's conceptions of physiological equilibrium form an attempt to extend Ribbert's doctrine on mathematical lines.

Now if this were all, it should be easy to produce new growths by the experimental isolation of cells from their natural connexions. Such endeavours have been made, but only with occasional success. Imbued with the idea that a detachment of epithelium from its basement-membrane formed the essential starting-point of a cancer, Dr. Lambert Lack in 1898 crushed and scraped up the ovary in two rabbits, distributing the products over the peritoneal cavity of the animal itself. In one of the two he got a positive result: the animal died about a year after the original operation, with indisputable carcinoma of the peritoneum and pleura, and secondary growths in the viscera. The present writer can vouch, from personal examination of the specimen, for the truly cancerous nature of the growth, which was columnar-celled. But inasmuch as the experiment has never been successfully repeated there must be a doubt as to the causal connexion between the operation and the neoplasm. Lubarsch records one successful experiment of his own: he implanted a portion of a rabbit's submaxillary gland at the upper pole of its kidney. After four months the animal wasted and died: the kidney, which had been absolutely normal at the date of operation, was found to present a tubular adeno-carcinoma. The growth had no histological characters to suggest an origin in salivary gland-tissue, and Lubarsch himself does not lay much stress on the experiment. Birch-Hirschfeld and Garten mashed up very young embryos and injected them into the livers of animals of the same species. They used goats, rabbits, hens, frogs, etc., and obtained some positive results in the case of rabbits and hens: cartilaginous tumours, and in one case a mass of retinal epithelium with pigment, were produced in the liver: even in the lungs small foci of cartilage were occasionally found. The experiments proved the power possessed by embryonic tissues of developing up to a certain point in another organism of the same species, but the tumours lacked the true autonomy of genuine

neoplasms, since in every case, when the animals were allowed to live, the growths underwent degeneration and atrophy: in one case they persisted for nearly a year, but this was the extreme limit.

The occasional apparent success of experiments such as these serves only to bring into relief the very much larger number of similar efforts which have had an absolutely negative result. Yet if Ribbert's conception of liberation from tissue-restraint lay truly at the root of the matter, the percentage of successes should have been a high one. Marchand has argued, with some justice, that the essence of tumour-causation must lie not so much in the dislocation of cells from their natural connexions as in the persistence of a germ capable of proliferation. It would seem necessary to postulate some profound biological alteration in the cells constituting a new growth, in order to explain their independent and parasitic characters. It may be that the solution of the problem lies in one or another of the biological speculations which have recently been put forward as to the origin of new growths, and which must now be considered.

Biological Suggestions.—It is a striking illustration of the interdependence of the different sciences that within the past few years suggestions as to the essential nature of new growths should have originated from workers in fields apparently outside pathology—from biologists, embryologists, and cytologists. Biological views of tumour-formation are necessarily speculative and difficult of direct proof; nevertheless they are well worthy of close attention, and, in order that they may be intelligible, it is needful to state shortly the more important details of the life-cycle now generally accepted by biologists.

According to the views of Weismann, inheritance is from the parent germ-cell, not from the parent-body. The body is an offshoot of the germ-cell—merely the bearer of the germ-cells of future generations; the direct continuity of the germ-plasm from one generation to the next seems well established. In the lower plants and in some of the lower animals a well-marked "alternation of generations" occurs, the complete cycle being formed of a sexual and an asexual phase. In the higher plants the sexual generation is reduced to very small dimensions: the visible self-supporting plant is the asexual generation; the sexual generation consists of a few cell-divisions alone, carried out within the embryo sac and in the pollen mother-cells. It has even been suggested that the last rudiments of an alternation of generations are traceable in the higher animals, in the four cells produced by the oögonium and spermatogonium respectively. Be this as it may, it seems clear that throughout both animal and vegetable kingdoms there is a uniform alternation in the process of mitotic division. The cells which constitute the body proper exhibit a definite number of chromosomes in indirect cell-division, constant for each species. The germ-cells, at a given moment in their history, undergo heterotype mitosis, in which the chromosomes are reduced to half the somatic number—an obvious provision for maintaining constant the number of chromosomes in the fertilised egg. When once heterotype

mitosis has occurred, the somatic number of chromosomes can only be restored by a process of conjugation. Any cell-divisions which intervene between the heterotype division and such conjugation must be carried out with the halved number of chromosomes, even though in other respects they conform to the somatic pattern: such are termed "homotype" mitoses. Now in the lower plants the homotype or post-heterotype series of cell-divisions may be very extensive and may constitute an independent and self-supporting individual, permanent in the mosses, though already reduced to a temporary prothallium in the ferns. In the higher animals the post-heterotype divisions are reduced to the two by which the oögonium and spermatogonium respectively give rise to their four daughter-cells. Tissue in which reduced division occurs is thus stamped as reproductive tissue—eminently and directly reproductive in the case of higher animals and plants, more indirectly so where an obvious alternation of generations can be traced.

The fertilised ovum must evidently contain the potential rudiments of every tissue in the future body. It is probable, in spite of the doctrines of Roux and Weismann, that this is also true of the earlier blastomeres produced by its segmentation, for if, in the course of the first two or three divisions, the blastomeres be isolated experimentally, it has been found that in certain cases complete but dwarf embryos may arise from them (echinoderm, amphioxus, frog). Nevertheless there is good reason for believing that, as the embryo unfolds and as the different cell-groups become specialised, the properties of the cells become as it were sorted out, so that in the end the adult cells possess only the potentialities of their own kind of tissue. The only exception to this rule is formed by the germ-cells, which retain unimpaired their entire ancestral heritage. In one case (Ascaris) Boveri was able to bring forward morphological evidence of this, for he showed that all the somatic nuclei lose a portion of their chromatin, the cells destined to form the germ-cells alone retaining the full amount handed on by the parent.

Now it is quite certain that the cells of which a tumour consists are lineally descended either from the ovum from which the bearer of the tumour has developed, or from some other ovum or equivalent germ-cell accidentally included. It seems probable that the nature of the tumour which arises may vary with the stage of development at which the tumour takes its origin. In the case of the teratomas, composed of many different tissues, the primal rudiment must be either a germ-cell (or its equivalent) or a very early blastomere; while in the case of an innocent histioid or organoid tumour we should more naturally look for the origin of the rudiment at a later stage of development, when the cells had already become specialised. Neither supposition would, however, explain the peculiar properties of malignant growths: it has been suggested that these may take origin in tissue belonging to some predatory stage of development.

The only tissue in normal development which possesses eminently

predatory powers is the trophoblast. The observations of Peters, on the early stages of the human ovum *in utero*, show that the chorionic epithelium does actually behave as a malignant neoplasm within a restricted area of the maternal tissues. There is a fair consensus of opinion that the highly malignant deciduoma, or syncytioma malignum, owes its origin to this trophoblast, and it has been pointed out that the disease is more apt to arise when the embryo has perished at an early stage of development. Dr. Ritchie has described a condition indistinguishable from chorion-epithelioma in connexion with a dermoid cyst of the mediastinum: similar tumours have been found in the testis. There is hence good reason for supposing that some malignant tumours may originate in the trophoblast, and it is natural to explain their malignancy by pointing to the parasitic nature of the tissue in which they have arisen.

There are those who go further than this and would identify all malignant growths with the trophoblast. Dr. Beard, for example, on embryological grounds, professes to see no difficulty in the problem of the origin of cancer. For him a malignant growth is simply an irresponsible trophoblast—an asexual pre-embryonic stage of development—a life-cycle with the embryo omitted; he traces it to one or another of the rudimentary germ-cells which his researches have shown habitually to go astray in the course of development. Few pathologists will assent to so sweeping a generalisation, nor are Dr. Beard's views as to the essential nature of the trophoblast generally conceded even by embryologists. It is clear that some malignant growths present "epithelial" and others "connective-tissue" characters, pointing to an origin later than the differentiation of the primary germinal layers. Those who have most closely studied the very early stages of cancer trace the descent of the cancer-cells from normal adult epithelium, and this on very convincing ocular evidence. Nevertheless there is force in Dr. Beard's dictum that "a neoplasm is a futile attempt to repeat a greater or lesser portion of the cycle of normal development."

The discovery by Professor Farmer and Messrs. Moore and Walker of heterotype and homotype mitosis in malignant growths is one of manifest significance, inasmuch as such types have been hitherto found, in the normal body, only in reproductive tissue. It is natural that we should attempt to correlate it with the intense reproductive activities exhibited by such tumours, and it is tempting to go further and associate their eminently parasitic character with the known parasitic tendencies of the rudimentary gametophyte in higher plants. These authors point out that "in higher animals and plants the post-heterotype tissue, with its own independence of organisation, behaves towards the parent tissues as a neoplasm. It would be pathological if it were not a normal stage." They are careful to add that too much stress must not be laid on the destructive powers of the post-heterotype formation, since in the lower plants (such as mosses) it is the sporophyte which is parasitic on the gametophyte. Their suggestion as to the nature of the change in

malignant disease is that the normal somatic cells, owing to some unknown stimulus, have become converted into cells having the characters of reproductive (not embryonic) tissue. It is a suggestion as to the nature, and not as to the cause of the change. At present, however, we have scarcely sufficient data for the assumption that heterotype mitosis is confined to malignant growths. And even if this should prove to be the case, there is no very striking evidence that in the higher animals reproductive tissue possesses eminently parasitic properties. Tumours cannot be produced by the artificial transplantation of portions of the sexual glands. The experiment of Dr. Lambert Lack, already alluded to, is the solitary successful instance, and may have been an accidental coincidence. We are not, therefore, much helped by this discovery of Farmer, Moore, and Walker towards any apprehension of the actual cause of malignancy, though we may hope that it is a fact which will contribute towards the successful solution of the problem.

The view which has recently been advocated by Drs. Bashford and Murray as to the nature of malignant growths is based in part upon the discovery of Farmer, Moore, and Walker, but is chiefly the outcome of their own comparative researches on cancer in the lower animals and upon the course of implanted epithelioma in mice. They point out that the growth of this neoplasm, transferred from mouse to mouse, is practically unlimited, yet that even in remote generations it preserves its general histological characters unaltered, while the somatic number of the chromosomes is maintained. For considerable periods no heterotype mitoses can be detected; but at recurring intervals they appear, usually in scanty numbers. It is at such times that these observers have detected nuclear conjugations, and they suggest that the restoration of the somatic number of chromosomes, thus brought about, serves as the starting-point for a new generation of cancer-cells. The growth of the neoplasm, whether continuous, metastatic, or artificially transplanted, would thus be resolved into a series of cycles, to the number of which there is no apparent limit, each cycle having heterotypical mitosis as its terminal phase, and conjugation of the reduced daughter-nuclei as the initial phase of the succeeding cycle. Such a hypothesis would be a legitimate inference from the observed facts; but in order to explain the primary origin of a malignant growth it is necessary to make assumptions of a more general nature. The suggestions which Drs. Bashford and Murray put forward are, shortly, as follows. It is universally admitted that heterotype mitosis is a terminal phase in the life-history of the reproductive cells of animals. It may be that in other tissues which are nearing the limits of their proliferative powers a similar heterotype mitosis may sometimes occur—perhaps as a last tradition of the times when, amongst unicellular organisms, preparations for rejuvenescence were needful in every senile cell. A chance nuclear fusion between somatic cells which had thus undergone reducing division might form the starting-point of a new organism, which would differ from that

resulting from the fusion of sperm and germ in normal reproduction in this respect that, instead of containing all the chromatin-heritage of the species, and thus the potentiality of developing into a complete individual, it would consist of a single type of cell only—that represented by the special chromatin-heritage of the differentiated cells from which it had arisen. It would be a "one-tissue" organism, whether epithelial, endothelial, or connective-tissue in its nature, and would, perforce, be parasitic, for no single tissue could maintain an independent existence.

Drs. Bashford and Murray's conception is thus seen to rest in part upon certain definite observations made in their study of the growth of artificially propagated malignant tumours in mice, and in part upon an assumption not as yet verified by actual observation, to wit, the spontaneous occurrence in the intact organism of heterotype mitosis and subsequent nuclear fusion in tissues other than those concerned in normal reproduction. It would satisfactorily explain the autonomy of malignant growths, their unlimited powers of growth, and also their age-incidence. But inasmuch as innocent tumours are also autonomous, and cannot be sharply defined from those of malignant nature, it is manifestly an incomplete hypothesis unless it serves to explain these also. Hitherto heterotype mitosis has not been demonstrated in innocent growths, though it would be premature to deny its possible occurrence. If we accept Drs. Bashford and Murray's speculation as to the primal inception of an autonomous new growth, it is tempting to suggest that, while innocent and malignant tumours may alike *originate* in the nuclear fusion of "reduced" cells, the degree of malignancy may depend upon the *recurrence* of this process. No one has yet seen any indication of the phenomenon in an innocent tumour, and it may be that such growths owe their benign course to its absence, behaving, save for their autonomy, as any other mass of normal tissue. Amongst malignant tumours, on the other hand, heterotype mitosis is now shown to occur, and in one case—the only one in which an attempt has been made to prosecute an extended cytological research throughout several generations—it has been shown to recur. It may prove that the frequency of recurrence—*i.e.* the shortness of the cycle—may determine the clinical malignancy of any given form of tumour. Such a conception, speculative though it be in the present state of our knowledge, would at least extend Drs. Bashford and Murray's view to innocent growths, and would serve to explain the varying degrees of malignancy of different tumours, the transitions from innocent to malignant growths, and even the origin of a malignant from an innocent one.

These biological speculations afford pregnant suggestions towards a theory of the essential nature of tumours. We are, as it were, on the verge of some great generalisation which shall make everything clear, but at the moment we see through a glass, darkly. The hypothesis which seeks to explain new growths as due to an external parasite has been seen to lack convincing evidence: it would make clear the primary causation of such growths, but would fail to explain their course and

behaviour in the body. The recent biological hypotheses which have been above outlined, while offering a reasonable explanation of the parasitism and autonomy of malignant growths, with one exception scarcely touch the primary question of their causation. And even the conception of the fortuitous nuclear fusion of post-heterotype cells is not based upon any direct evidence. For the present we must be content to look upon new growths as autonomous structures, of the rank of parasitic "individuals," but wherein lies the secret of their individuality is for the future to disclose.

Prognosis and Treatment.—In the absence of any conclusive evidence as to the causation of new growths, prognosis and treatment are necessarily empirical, and must be considered together. The limits of this article preclude any but a brief reference to the subject.

Experience has abundantly shown the wide difference in prognosis between innocent and malignant growths, as defined in the preceding pages. Our ideas of innocency and malignancy are in fact based upon our experience in this respect. An innocent growth, as its name implies, does not tend to shorten life except in special and, as it were, accidental circumstances. Amongst such circumstances may be mentioned the following:—The growth may slowly attain so enormous a size that it mechanically impedes the functions of important organs and interferes with the nutrition of the body. Multilocular ovarian cystomas have been known to grow to a weight exceeding a hundred pounds; it has even been noted, after operation, that the patient from whom the tumour had been removed weighed less than the tumour itself. Such cases die if unrelieved by operation. Comparatively small innocent tumours may chance to interfere with the function of a vital organ; cerebral gliomas and meningeal endotheliomas may prove fatal when only of moderate size; uterine fibroids, by obstructing labour, may destroy the patient's life. Lastly, there is the possibility of the development of a malignant growth from an innocent one. The origin of melanotic sarcoma from an innocent mole is one of the best known and most frequent examples of this, but similar cases are far from unknown elsewhere. In the museum of St. Bartholomew's Hospital are specimens of mixed parotid and mixed palatine tumours which, after an innocent course extending over many years, gave rise to malignant endotheliomas; in the same collection is a carcinoma arising in the centre of a fibro-adenoma of the breast, and still completely surrounded by the innocent tumour-tissue. On the other hand, innocent tumours tend, more than malignant ones, to become stationary in their growth, as, for instance, many lipomas and papillomas; the behaviour of uterine fibroids at the menopause is another instance in point. But although the majority of innocent tumours do not in any way threaten life, they are commonly removed by the surgeon when possible, if only to make sure that they are innocent, and such operations are almost invariably attended by complete success. There is one circumstance which should always lead to prompt removal—namely, sudden and marked increase in the size of an innocent growth after a

long period of inactivity; it is in such cases that the development of a malignant growth may be feared.

In malignant growths the outlook is of a much more serious character. The prognosis naturally varies with the degree of malignancy of the growth, and with the stage at which its nature is recognised. Cases are not absolutely unknown in which the progress of a tumour, believed on histological evidence to be malignant, becomes arrested; indeed such tumours have been known to disappear, as in the cases of so-called "withering sarcoma." Such occurrences, however, come under the heading of curiosities of pathology, and must not be allowed any weight in forming a prognosis. In every case of malignant disease accessible to the surgeon and seen at a sufficiently early stage for complete removal, a free excision is indicated, for there can be no doubt that the knife offers by far the most hopeful prospect of a cure. Moreover, the more extensive and radical the operation the smaller is the chance of recurrence. There are certain situations in which the hope of freedom from recurrence is greater than in others; the lip and the rectum are such places. The nature of the growth has an important influence on the matter; recurrences are practically the rule with the more anaplastic types of sarcoma. It is impossible to give figures of any general value; probably the statistics of no two surgeons would correspond; but many can show a very fair percentage of cases in which an apparent cure of malignant disease has been effected by early and free excision.

There must always be a proportion of cases of malignant disease which are inaccessible to operation, or are seen at too late a stage to offer any hope of complete removal. The prognosis in such inoperable cases is naturally of the gravest: they offer the field for the alternative methods of treatment which are continually being brought forward, and some of which appear to have met with a slight measure of success. A malignant growth which cannot be reached by the knife is scarcely more accessible to caustics. It is to be feared that the same criticism applies to the more recent attempts to destroy malignant growths by intense light, by Röntgen rays, and by the emanations of radium, though it is perhaps too early to pronounce any final verdict on these. It is not clear that the living cells of tumours are much more sensitive to such agents than are the normal tissues amongst which they are growing.

The treatment by erysipelas toxin has yielded, in the hands of Coley, somewhat more hopeful results. It has been established on clinical grounds that an attack of erysipelas sometimes produces an improvement or even a cure in cases of malignant disease. Erysipelas has been deliberately induced, by inoculation of the streptococcus, in a number of inoperable cases. Eschweiler has summarised 59 cases of malignant disease associated with spontaneous or induced erysipelas; of these no less than 25 per cent appear to have recovered, while 10 per cent died of the erysipelas. Inasmuch as Bacillus prodigiosus was known to exalt the virulence of streptococci, Coley was led to

employ a sterilised mixture of this bacillus with the erysipelas streptococcus. The preparation known as *Coley's fluid* is a broth culture of the two organisms grown together and sterilised by heating to 58° C. Subcutaneous injections of this fluid are employed; in cases of carcinoma they have proved fruitless, but in sarcoma, and especially in spindle-celled sarcoma, distinct successes are claimed not only by Coley but by others who have used his method. Coley treated 22 cases of spindle-celled sarcoma, of which 10 disappeared and all the rest improved; but of 86 round-celled sarcomas, only 3 were cured, while 38 improved. In a certain number of cases recurrence took place, but out of a total of 148 sarcoma cases, all inoperable, he claims 12 per cent of final successes. One per cent of deaths is recorded as due to the treatment.

A method of treatment which has been occasionally followed by success in inoperable cases lies in *removal of the ovaries*, together with the administration of thyroid extract, as advocated by Dr. Beatson. The cases which he records, and those which have since been recorded by others, as benefited, are few in number, and have all been cancers of the female breast. It would be rash to argue from the scanty facts at our command that the ovaries, much less the testes, as Dr. Beatson is also inclined to suggest, exercise any specific influence on epithelial proliferation in general. Nevertheless the known influence which removal of the sexual glands exerts upon secondary sexual characters renders it far from improbable that removal of the ovaries should exercise a distinct influence upon the mamma, making for involution of tumours originating in its epithelium, if only by a diminution in the blood-supply. The method of treatment is one which may well be taken into consideration in inoperable cases of this special class, as it is stated that benefit is obtained in about one-third of the cases in which oöphorectomy has been performed. What share, if any, is taken by the thyroid treatment is less clear, but Mr. F. Page records a case in which apparent cure of recurrent cancer of the breast was produced by thyroid extract alone.

With the introduction of serum treatment for certain bacterial infections, and more especially with the discovery of cytolytic powers in suitably prepared sera, new hopes seemed to be held out as to the cure of malignant disease. Those who accepted the view of an invading micro-parasite had before them a method analogous to that which had already proved effective in some bacterial diseases, provided only that they could cultivate the parasite. So far no convincing results have been attained, and criticism would be premature. On the other hand, those who held one or another of the intrinsic hypotheses as to the nature of new growths had before them the problem of producing a cytolytic serum which should act on the cells of the new growth and not on those of the normal body. Looking at the facts of cytolysis as at present known, and at the strict limits of the inoculability of malignant growths, it must be confessed that the prospects of producing such a serum are not of the brightest. If, as seems increasingly probable, the cells of new growths are essentially the cells of the body perverted in their biological

properties, it is unlikely that any serum can be prepared which will possess the necessary limitations of action. A serum capable of cytolytic action upon a columnar-celled carcinoma of the rectum might well destroy at the same time the columnar epithelium of the rectum itself.

It would thus appear that in the treatment of new growths no striking advance has been made upon the ordinary methods of operative surgery. The more recent methods which have just been mentioned offer, at the most, palliation and respite, with an apparent cure in a certain small proportion of the cases. The matter is indeed one in which almost insuperable difficulties have to be overcome; the tendencies of recent research to refer new growths to fundamental biological changes in the tissue-cells themselves, far from simplifying the prospects of successful prophylaxis and treatment, would appear to render them still more remote. A heterotype mitosis may prove a more elusive foe than a pathogenetic yeast.

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[*Note.*—The literature of new growths is so enormous that the only references here quoted are to those authors whose views or statements have been referred to in the text, and to those works which the writer has had especial occasion to consult.]

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CLINICAL EXAMINATION OF THE BLOOD AND ITS SIGNIFICANCE

By J. H. DRYSDALE, M.D., F.R.C.P.

Introduction.—In the last few years the value of the clinical examination of the blood has become increasingly recognised, and a practical acquaintance with the necessary technique has therefore been more widely diffused. As a result, it is now generally conceded that blood examination is as important a method of clinical diagnosis as the use of the thermometer or the stethoscope. Even now, however, its full advantages are seldom realised in practice; and casual scattered observations too often take the place of the routine examination, which only can supply the data necessary for the advance of our knowledge, or for enabling us to use it to the fullest advantage. For the correct interpretation of these data a knowledge of the limitations of the method is also necessary.

In certain conditions, in leukæmia and pernicious anæmia for instance, examination of the blood will often of itself suggest the diagnosis; but even in these cases there are occasional sources of error; for example, the periods of remission which occur in leukæmia, and the occasional similarity in the blood-changes in infection with Bothriocephalus latus and in pernicious anæmia. On the other hand, in these and many other conditions the diagnosis may be said to depend altogether on the result obtained by the examination of the blood, and without this, to partake only of the nature of a pious opinion. It should be clearly recognised, therefore, that blood-changes are in every case symptomatic merely, and no greater value should be attached to them; at the same time it must be allowed that they may be symptoms of preponderating worth without a knowledge of which the other symptoms leave us in doubt. Again, a "negative" result, that is, an absence of appreciable blood-changes, may be of as much value as a positive; for example, in deciding between the presence of typhoid fever and certain pyogenetic infections.

From these considerations it necessarily follows that no conclusion should be drawn in any case without: (1) an accurate knowledge of the clinical history and symptoms of the patient; and (2) a wide acquaintance with the conclusions already established by these methods of investigation.

It is impossible to draw up any scheme for the routine examination of the blood in every detail, since the points of primary importance will naturally vary in different cases. The methods which in our present state of knowledge yield the most fruitful results are:—

1. Microscopical examination of fresh blood.
2. Estimation of the amount of hæmoglobin.
3. Estimation of the number of red corpuscles.
4. Estimation of the number of white corpuscles.
5. Microscopical examination of fixed and stained preparations.
6. Blood-cultures for bacteriological purposes.
7. Examination of serum-reactions, especially for the presence of agglutinins.

Attention may also be directed to other methods, which, however, are less commonly used—sometimes because they are ill adapted for clinical work, sometimes because the results are not sufficiently reliable, or again, because the information to be gained is only of use in a limited number of cases. Such are:—

The estimation of the specific gravity of the blood.
The determination of the coagulation-time.
Spectroscopic examination.
The estimation of the degree of alkalinity, and many others.

Technique

To Obtain the Blood.—If, as most commonly happens, the amount of blood required for examination is not large, it may be obtained either from the finger or from the lobule of the ear. The finger is more easily

manipulated and controlled, and in some cases, as when the ear is very thin, more blood may be obtained from it, or from a toe, than from the ear. On the other hand, the lobule of the ear is but slightly sensitive even to a deep puncture, whilst, if sufficient blood is to be obtained without pressure, the necessary puncture in the finger is manifestly painful. On the whole, therefore, the ear is to be preferred, especially in young children, in whom it is an advantage that the manipulations are performed out of sight. The danger of infection of the wound either at the time of the operation, or subsequently, is in any case so exceedingly small that it may be almost neglected; but the instruments are so easily sterilised in the flame of a spirit-lamp or Bunsen burner that it is well to take this precaution. For ordinary non-bacteriological blood-examination it is not necessary to sterilise the skin, but it should nevertheless be clean and dry—clean, so that particles which might simulate pathological appearances may be excluded; dry, so that alterations in the constituents of the blood may be avoided. Gentle cleansing with ether will meet both these requirements. The blood should be obtained with as little disturbance of the part as possible. The application of ligatures, squeezing, or vigorous rubbing must particularly be avoided, or the composition of the blood will be altered, and the results vitiated. Special stabbing implements are provided with many instruments, but an ordinary straight Hagedorn needle (No. 4 is a convenient size) is as good as, if not better than, anything else. Ordinary sewing-needles are much less efficient without being any less painful. Ehrlich recommends a steel nib with one point broken off. The skin of the part chosen having been put on the stretch, a prick sufficiently deep to cause a free flow of blood is made; the first two or three drops are wiped away, and the succeeding ones used for examination. A sudden stab with a quick withdrawal of the needle is less painful than a more deliberate puncture. When a larger quantity of blood is required it must be removed from a vein by means of a syringe. For certain chemical examinations and the like it is unnecessary to take extreme precautions against bacterial contamination, but this care is of course essential when the object in view is to demonstrate the presence of bacteria. The most convenient method is to use a syringe of about 10 c.c. capacity. Many suitable syringes, made entirely of glass and readily sterilisable by boiling, can now be obtained. The needle should be of medium stoutness. The skin of the patient as well as the instruments having been carefully sterilised, and any antiseptic carefully washed away with sterile water, the needle attached to the syringe is thrust obliquely through the skin in a direction nearly parallel to the long axis of the vein. If the vein has been previously compressed by an assistant there will be no difficulty in getting the needle into the vein; the most frequent error is to pierce the vein altogether and so enter the tissues beyond. Any amount of blood up to the full capacity of the syringe can now be withdrawn. The blood should be divided between several culture tubes containing the media most suitable

for the growth of the organism whose presence is suspected. A simple pad and bandage are applied at the seat of the puncture after the needle is withdrawn.

A positive result is naturally more likely to be obtained when large quantities of blood are used, but many such results have been obtained with small quantities taken in a capillary pipette, containing ·5 c.c. or less, from puncture of a finger. In such cases the risk of contamination of the skin is very largely increased; but notwithstanding these drawbacks, the method is of considerable value when the apparatus necessary for taking larger quantities is not available. After sealing the pipette, too, the material can readily and safely be sent to a distance.

Any attempt to demonstrate the presence of bacteria in the blood by means of the direct examination of stained films, except in the rarest instances, as in some cases of septicæmic plague or anthrax, is so much waste of time.

The Estimation of Hæmoglobin.—The more accurate methods of estimating the amount of hæmoglobin present in the blood, by chemical analysis or by the spectro-photometric method (Vierordt, Hüfner), are, owing to their elaborate technique, not adapted for clinical purposes, and in practice the methods in common use are all colorimetric in nature. The instruments thus used are those of Gowers and von Fleischl. In each case improvements have been suggested, and the Miescher-Fleischl and Haldane's modification of Gowers' apparatus are certainly to be preferred to the originals.

Von Fleischl's Hæmoglobinometer consists of (1) a cylindrical, glass-bottomed cell (A, Fig. 49), divided into two halves by a vertical partition.

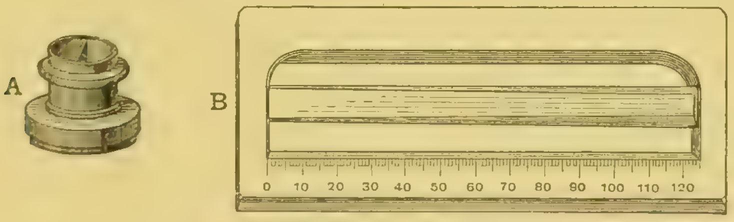


FIG. 49.—Von Fleischl's hæmoglobinometer.

(2) A metal frame (B, Fig. 49), which carries a narrow wedge of red-coloured glass. The tint of the coloured wedge, starting with clear glass, varies from a pale carmine at the thin end up to a deep purplish red at the thick end. The metal frame is correspondingly marked in percentages from 0 to 125. (3) A stand (C, Fig. 50) furnished with a stage (*a*), having in it a circular hole (*b*) near its centre, and a second smaller oval opening (*c*) behind the circular one. Beneath the stage is a flat, white, plaster disc (*d*), fixed like the mirror of a microscope, to act as a reflector. The metal frame fits into grooves (*ee*) on the under surface of the stage in such a way that the graduated scale lies under the smaller oval opening and the coloured wedge under the inner half of the circular opening. Any portion of the wedge, with its correspond-

ing scale, may be moved by means of the screw (*f*) under their respective openings. (4) Small capillary pipettes (D, Fig. 51), mounted in metal handles and of measured capacity, varying with the individual instrument. These pipettes are for measuring the blood, and in each case hold the amount that ought, on the regular dilution of blood with normal hæmoglobin-percentage, to correspond in tint with that of the wedge opposite, 100 per cent on the scale. The pipettes and the stand are marked with the cubic capacity of the pipettes. (5) A fine-pointed glass dropper (E, Fig. 51) for use in washing out the pipettes and in filling the two sides of the cell. To use the instrument, partly fill one side of the cell with distilled water by means of the dropper. To a drop of blood, obtained with the usual precautions, carefully apply one end of a small pipette, which, if absolutely clean, will then fill itself automatically. The filling will be assisted by holding the pipette horizontally, or inclined a little downwards. Care must be taken that the pipette is filled exactly, the ends of the blood column being neither concave nor convex. Any blood adhering to the outside should be carefully removed with a piece of filter-paper. The pipette is then transferred to the side of the cell containing the water, and moved briskly to and fro in order to wash out the blood, and the washing completed by means of the dropper. The handle of the pipette may be used to mix the blood and water thoroughly, and then the cell is completely and accurately filled on both sides, care being taken that the fluid on either side does not flow across the thin dividing partition. The cell is now placed in the circular opening in the stage in such a position that the side containing distilled water only lies over the coloured glass wedge, that containing the blood mixture lying to the outer side. With some low-powered *artificial yellow* light (daylight, electric, or incandescent light are not suitable) directed upwards by the reflector, the blood mixture is now matched as to its depth of colour with the coloured wedge, and when this is accomplished the result is read off on the scale in percentages of the normal. The matching should be done in a dark room. The best light is that obtained from a small candle placed a foot or so away from the stage. With low readings especially, the less light used the more exact will be the result. Light should be

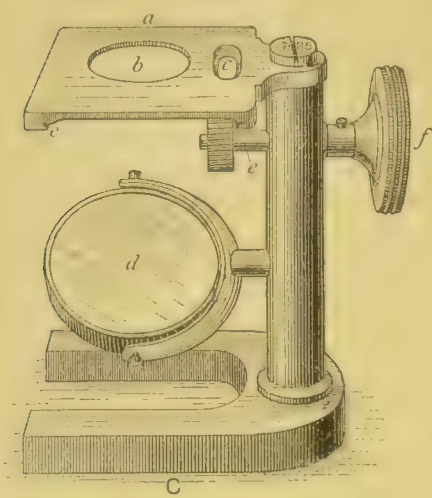


Fig. 50.—Von Fleischl's hæmoglobinometer.

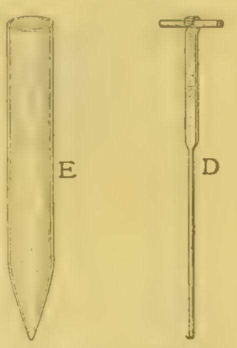


Fig. 51.—Von Fleischl's hæmoglobinometer. Capillary pipette and dropper.

prevented from reaching the eye directly, by using as a cylinder any convenient roll of opaque paper; this is fitted over the cell, and in making the observations the eye is applied to the other end. It is well to look sideways at the stage, so that the blood and the wedge may fall on the lateral halves of the retina rather than on the upper and lower half (Cabot). The matching should be completed rapidly, with frequent rests to avoid fatiguing the eye, and at least two readings should be made. In one the observation should be commenced with the wedge obviously paler, in the other obviously darker, than the diluted blood; then the wedge should be moved rapidly, by turning the screw (*f*) till the match is apparently exact. The mean of these two readings should be taken. This process may be repeated with each eye, if the observer has normal eyes, or several pairs of readings should be taken with the same eye. The instrumental error is least marked at the middle of the scale, and with anæmic bloods it is best to use two or even three pipettes of blood, dividing the result. For the same reason it is well in choosing an instrument to select one with pipettes of a capacity between 7·5 and 8·5 c.mm. Low capacities in the pipettes are especially to be avoided. In some of the older instruments the readings for the average healthy man were unduly low, from 85 to 90 per cent, but in the more recent ones the average is 10 degrees or more higher. The probable explanation of this lies in the empirical method by which the instrument is standardised (11).

The great objection to the instrument lies in the coloured wedge, for the portion which compares at any given time with the blood has a range of 18 to 20 per cent, so that the extreme tints in view vary, for example, from 40 to 60 per cent. Further, in filling the cell completely, unless care is taken, the fluid may flow across from one side to the other and completely vitiate the observation.

The instrument should, like all other instruments used for blood-examination, be cleaned immediately after use. The cell unscrews, and can be easily cleaned in running water and dried. The pipettes should be washed in water, alcohol, and ether. A needle and cotton will readily remove the blood from them should coagulation have taken place, but they are fragile and easily broken.

In *Miescher's Modification of von Fleischl's Instrument* most of the defects of the original Fleischl have been remedied. The dilution of the blood is made in a pipette (A, Fig. 52) similar to that of the Thoma hæmocytometer; this ensures greater accuracy in the measuring and mixing. In addition, by means of graduations in the pipette, varying dilutions may be made to suit the standard of the blood under examination. The capillary portion of the pipette is marked in three places—$\frac{1}{2}$, $\frac{2}{3}$, and close to the bulb $\frac{1}{1}$. If blood is drawn up to any of these marks, and the pipette filled with diluting fluid up to the mark immediately above the bulb, the degree of dilution obtained will be respectively 1 : 400, 1 : 300, and 1 : 200. In the majority of cases the 1 : 300 dilution is most suitable, but when a considerable degree of anæmia is present the

dilution used should be 1 : 200; on the other hand 1 : 400 will serve best if the hæmoglobin approaches or surpasses the normal amount. The diluting fluid recommended is a 1 per cent solution of sodium carbonate which gives a clear solution; but distilled water may be used. The apparatus possesses two cells (B and C, Fig. 53), one with a depth of 12 mm. and the other with a depth of 15 mm. Both cells should be used in every estimation and serve to control each other. The dividing partition (*a*) in each cell is carried up above the top, and in this way any escape of fluid from the one side to the other is prevented. Partly owing to the filling in (*b*) of the extreme ends of the cells, and partly by means of a diaphragm (D, Fig. 53) fixed over the cells before the reading is taken, the section of the coloured wedge in view at any one time during the performance of an estimation does not cover more than 3 degrees on the scale. This gives what is practically a single tint for comparison. The coloured wedge is much more carefully standardised. The collection, dilution, and mixing of the blood are done as in using the hæmocytometer (*q.v.*). After the neat diluting fluid has been expelled from the capillary portion of the pipette, one side of each of the cells is completely filled, or slightly overfilled, with the blood mixture, and the opposite side is similarly filled with water. A special grooved glass cover (E, Fig. 53) is then slid along the projecting partition, and finally a diaphragm is placed over each cell. The matching is completed in exactly the same way as in the original instrument. The reading obtained with the shallower cell must be multiplied by $\frac{5}{4}$, and the mean of this figure and that obtained directly with the deeper cell is taken as correct. A table accompanies the instrument for translating the results secured into the amount of hæmoglobin present. The instrument gives very accurate results, and does not require the possession of any great skill for its use. The ordinary von Fleischl cell and measuring pipettes are also supplied with the instrument.

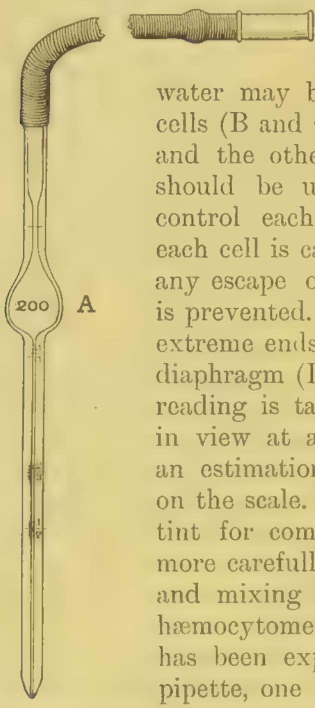


Fig. 52.—Miescher's modification of von Fleischl's hæmoglobinometer.

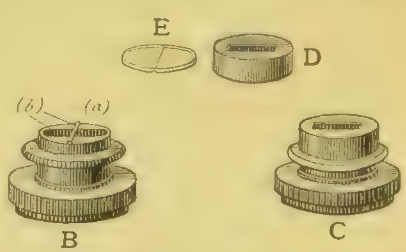


Fig. 53.—Miescher's modification of von Fleischl's hæmoglobinometer. Cells, diaphragm, and grooved glass cover.

Tallquist's Hæmoglobinometer.—Ehrlich and Lazarus draw attention to the value of a very simple method for roughly estimating the percentage of hæmoglobin at the bedside. A small drop of blood is allowed to distribute itself in a thin layer on a piece of linen or filter-paper. With a little practice useful conclusions can be drawn as to the degree of

anæmia. Great accuracy is not claimed for the method. Tallquist, following up this indication, has contrived a simple method by which more accurate results may be obtained with no greater trouble. The whole apparatus consists of a book with sheets of specially prepared white filter-paper, each perforated so that convenient portions may be detached, and a coloured lithograph scale graduated in ten tints from 10 per cent to 100. In the centre of each tinted section is an opening in which the blood-stain when ready may be placed for the purpose of matching. A fair-sized drop of blood is allowed to soak slowly and evenly into a portion of the specially prepared filter-paper. As soon as the blood-stain has lost its humid gloss, and before drying from exposure has taken place, it is held against a pad of filter-paper and compared with the scale. If it should match any one tint exactly, the reading is complete. If it should come between any two, the mean of those two is taken as the reading. The lithographed scale is prepared by copying the colour of the blood, taken on filter-paper, of patients whose hæmoglobin-percentage has previously been estimated with the Miescher-Fleischl instrument. Readings can only be taken by daylight. According to Tallquist the error does not exceed 10 per cent. The method is so simple and rapid that notwithstanding its inaccuracy it is useful in the out-patient room, for instance, as a control to the ordinary facial diagnosis of anæmia, or as a fairly satisfactory measure of improvement. Indeed, if constantly employed, it is probable that the error will not exceed that incurred by the unpractised in the use of more exact but to them less familiar methods. The authorised scale seems to be rather flattering to British hæmoglobin.

Haldane's Modification of Gowers' Hæmoglobinometer consists of two tubes (A and B, Fig. 54) having the same internal diameter. The liquid in A is a 1 per cent solution of blood containing the average percentage of hæmoglobin found in the blood of healthy male adults, and having an oxygen capacity of 18·5 per cent as determined by the ferricyanide method. The solution is saturated with carbonic oxide and the tube hermetically sealed. It is both definite and permanent. The tube B holds 2 c.c. when filled, so that the inside is completely wetted, and the liquid stands at 100 mark after allowing half a minute for the upper part to drain. The tube is graduated from 10 to 130 in percentages of 2 c.c. The capillary tube (C, Fig. 54) holds 20 c.mm. (= ·02 c.c.) to the mark. Hence if blood taken up to the mark is ejected into B and diluted with water so that, after mixing, the liquid stands at the mark 100, a 1 per cent solution of the blood is obtained; and this solution, if the blood be exactly normal, will, after saturation with carbonic oxide or coal-gas, have the same tint as the standard solution

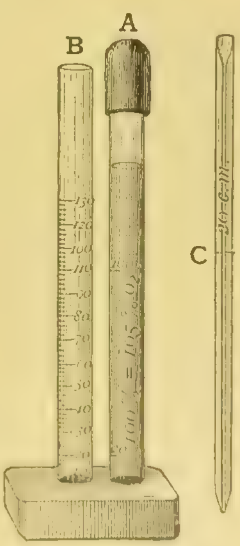


Fig. 54.—Haldane's modification of Gowers' hæmoglobinometer.

in A. If the blood contains more, or less, than the normal proportion of hæmoglobin, the dilution required to match the tint of the liquid in A will be proportionately greater or less. When the tints match, the height of the liquid in B will indicate the percentage of the normal of hæmoglobin present in the specimen. The bottle (D, Fig. 55) holds the water required for diluting the blood. The water can be added drop by drop with the help of the pipette stopper (*a*).

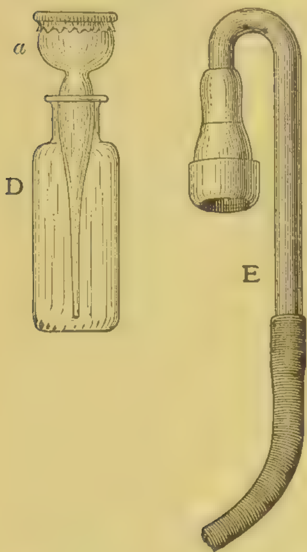


FIG. 55.—Haldane's modification of Gowers' hæmoglobinometer.

E (Fig. 55) is a small metal tube with cap for attachment to a gas-burner, and serves to deliver, through a short length of rubber tubing, gas for saturating the diluted blood with carbonic oxide.

Method of Use. — Sufficient water is first placed in the graduated tube B to dilute the blood as far as is possible with safety. A drop of blood is carefully obtained, and the capillary pipette filled up to the mark. The point of the pipette is wiped, and if the mark has been overshot, the excess of blood is got rid of by gently dabbing the point on a clean cloth. The blood is then gently blown out into the water contained in the graduated tube, where it sinks; the pipette is rinsed with the water in the graduated tube and withdrawn. The metal cap E is fixed on to a gas-burner, and the piece of rubber tube attached to it is introduced into the graduated tube till it almost reaches the level of the water, and gas allowed to pass for a few seconds. As the rubber tube is withdrawn (with the gas still passing) the end of the tube B is closed with the fore finger, and the hæmoglobin of the diluted blood is saturated with carbonic oxide by inverting the tube steadily a dozen times at least. During this manipulation the tube should be held in a handkerchief, otherwise it will become heated, and liquid is liable to spurt out when the finger is withdrawn. Water is now added to the blood mixture, drop by drop, with the pipette stopper, the tube after each addition being inverted, until the point is reached at which the tints of the liquids in the two tubes are absolutely equal. In judging of this equality the tubes should be held against the light from the sky, or, if artificial light be used, from an opal glass shade. It is also absolutely necessary to transpose the tubes repeatedly; otherwise serious errors may arise. The level is read off on the graduated tube after half a minute has elapsed since the last drop added was mixed with the rest of the liquid by inverting the tube. The observation is repeated after the addition of another drop of water, and if necessary another, until the point is reached when the tints are again unequal. The true result is the mean of the readings giving apparent equality. The error in any single determination ought

not to exceed 1 per cent. The result obtained is the percentage actually present of the average proportion of hæmoglobin in the blood of healthy adult men. The blood of healthy men, however, contains more hæmoglobin on an average than the blood of healthy women or children. Women give an average of 89 per cent. It must be remembered that the percentage of hæmoglobin at or shortly after birth amounts to about 110. This falls till about the sixth month, when it is only 70 per cent, and then gradually rises to reach the normal in adult life. An additional tube filled with picro-carmine jelly, as in Gowers' original instrument, can be obtained for use when coal-gas is not available. The picro-carmine jelly, as is well known, alters on keeping, but as Haldane points out, its value in terms of the carboxy-hæmoglobin solution may be determined from time to time, and the correction ascertained, by contrasting them with the same blood.

Gowers' hæmoglobinometer, the parent instrument of Haldane's, differs from it only in that the tube containing the standard solution is filled not with a solution of hæmoglobin but with glycerin jelly coloured with picro-carmine. Both instruments possess the merits of simplicity in use and construction. Haldane's has in addition the advantage of a standard solution which is definite, permanent, and can be used indifferently by daylight or artificial light. The disadvantage in both cases lies in adding just the right amount of water to obtain a match. Gowers' standard can only be used by daylight.

The *hæmoglobinometers of Oliver and of Dare* are used to a considerable extent, the former in this country, and the latter in America.

Of Dare's the writer has no practical knowledge, but it is strongly recommended by Cabot, Ewing, and other American authors as accurate and simple in use. It embodies the advantageous principle of using undiluted blood in the estimation. The coloured standard is made of glass tinted as in von Fleischl's instrument.

Oliver's instrument is an adaptation of the well-known tintometer of Lovibond. The standard scale consists of a series of discs of tinted glass representing accurately solutions of hæmoglobin of varying proportion. The instrument admits of great accuracy, but its use is attended by greater difficulties than the Fleischl-Miescher.

Estimation of the Specific Gravity of the Blood.—The specific gravity of the blood may be measured either by the direct or indirect method. Of the indirect methods that of Hammerschlag is the simplest and the one most commonly in use. The normal specific gravity of the blood is about 1060 for men and about 1056 for women. In a urinometer glass or other convenient vessel a mixture of chloroform and benzol is made having a specific gravity between 1055 and 1060. When the probable density of the blood to be examined is known beforehand the mixture may be prepared approximately of the expected standard. A medium-sized drop of blood is collected in a capillary pipette with a medium-sized bore and is allowed to fall gently into the mixture. If the blood floats, benzol must be added and the mixture stirred with a clean glass

rod. If the drop sinks, chloroform must be added. In either case the fluid must be added a few drops at a time and well mixed. When the point is reached at which the drop neither rises nor sinks in the mixture, the specific gravity of the fluid is taken with a urinometer, and this, of course, will equal the specific gravity of the blood. The vessel used must be clean and dry. Care must be taken to avoid admixture of the blood with air. The drop of blood must be allowed to enter the mixture gently or it will probably break up. The whole process must be carried out as quickly as possible. The test may be performed by preparing mixtures of different specific gravities, and adding to each a drop of blood till one is found in which the blood neither rises nor sinks, or the mean specific gravity may be taken of two mixtures, in one of which the drop rises and in the other of which it sinks. The method may also be used for ascertaining the specific gravity of the blood-plasma, serum, or of serous exudations.

The specific gravity of the blood is not of any great value so far as clinical examination is concerned, but it may serve as an indication of the hæmoglobin-percentage with which it runs parallel in the great majority of cases.

Hammerschlag has prepared a table showing the hæmoglobin-percentage corresponding to the different degrees of specific gravity :—

1033-1035	25·30
1035-1038	30·35
1038-1040	35·40
1040-1041	40·45
1045-1048	45·55
1048-1050	55·60
1050-1053	65·70
1053-1055	70·75
1055-1057	75·85
1057-1060	85·95

In Roy's method, of which Hammerschlag s is a modification, the fluid employed was a mixture of water and glycerin. In both the principle is the same, and the method has been largely used in this country by Drs. Copeman and Lloyd Jones. Fano had previously used a mixture of gum in the same way. This is not a very trustworthy method of estimating hæmoglobin, because of the variation of the other constituents of the blood, *e.g.* the plasma in dropsy and the leucocytes in leukæmia.

In Schmalz's method a thoroughly clean and dry capillary pipette is carefully weighed. It is then filled with distilled water and again weighed. After careful drying the pipette is filled with blood and weighed a third time. The weight of equal quantities of blood and water having been obtained, the sp. gr. of the blood is easily calculated. The pipette should not be too small or the differences in weight will be almost inappreciable. The method is very accurate, but requires a very sensitive balance and takes a considerable time to carry out.

The enumeration of the corpuscles in a given quantity of blood.—The underlying principle in all the methods in common use for counting the number of corpuscles in the blood is the same. A measured quantity of blood is diluted; the number of cells present in a portion of this dilution is estimated, and from the results obtained the number present in a given quantity of blood is calculated. It is not allowable to deduce from this any conclusions as to the total number of red cells present in the total volume of the blood or as to variations therein. The volume of blood is maintained within narrow limits in health, but such evidence as we possess points to much greater fluctuation in disease. In the present state of our knowledge on this point deductions should be limited to occasions where a comparison is made between several cases of the same disease or between the same case at different stages.

(1) *The Thoma-Zeiss hæmocytometer* is now used almost universally for counting the number of cells in the blood, and has replaced to a great extent the instruments of Hayem, Malassez, and Gowers. It consists of two graduated pipettes for measuring, diluting, and mixing the blood, and a counting-chamber. One pipette (A, Fig. 56) is formed of a thick-walled capillary tube (*a a*) expanded above into a bulb (*b*), which contains a small glass bead (*c*) to act as a mixer. Above the bulb the tube is again narrowed. The capillary portion below is divided into tenths (the division nearest the bulb is marked 1, the middle one 0·5), and its total capacity being taken as one, the bulb is made to contain 100 parts. Immediately above the bulb there is another mark, 101. The portion of the tube above the bulb is provided with a short length of rubber tubing, fitted with a bone mouthpiece to assist in the filling of the instrument by suction. The other pipette (B, Fig. 56) is similar in every respect except that its bore is larger, and the capacity of the bulb is only ten times that of the capillary portion. The corresponding marks above and below the bulb are 11 and 1.

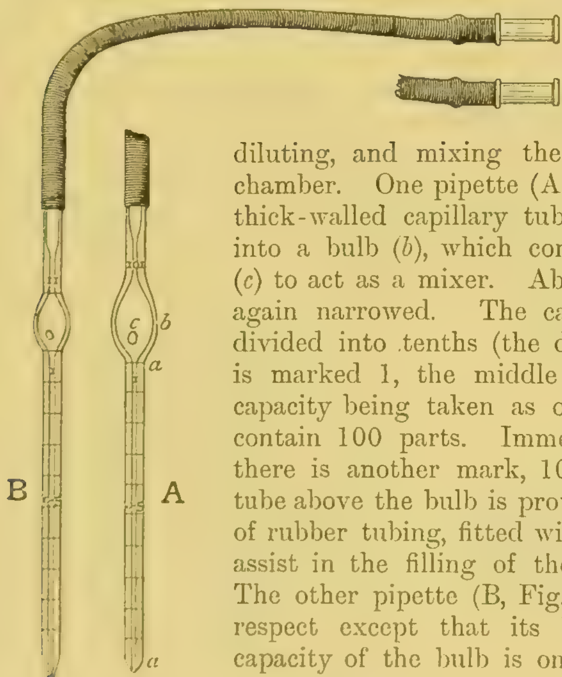


FIG. 56.—Thoma-Zeiss hæmocytometer pipettes.

The counting-chamber (C, Fig. 57) is formed of a thick glass slide (*e*, Fig. 57), on to which is cemented a square of glass (*a*) provided with a circular opening. In this central opening is fixed a circular disc (*b*), also of glass of lesser diameter, and of such a thickness that when the cover-glass is placed over the opening the depth of the space between the cover-glass and disc is $\frac{1}{10}$th of a millimetre. Owing to its smaller diameter a space surrounds the central disc of glass, forming a ditch or moat (*f*). Special cover-glasses are provided with the instrument.

To obviate any fallacy due to differences of pressure acting on the cover-glass and so altering the depth of the chamber, a groove (*c*) cut in the outer plate, as suggested by Meissen, allows of communication of the outer air with the counting-chambers. Rectangularly crossed lines (*d*)

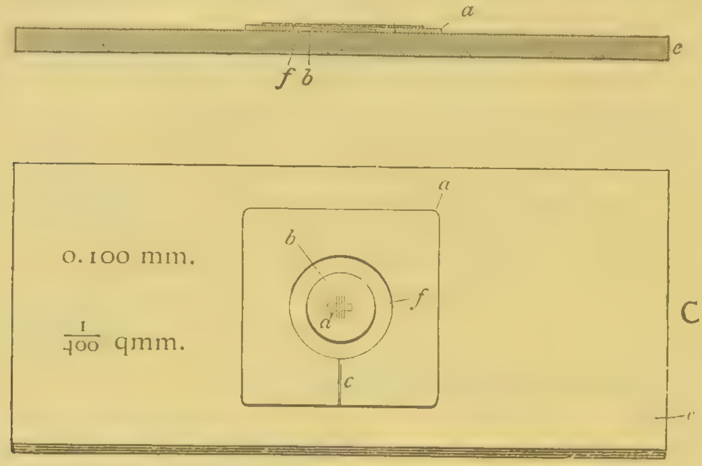


FIG. 57.—Thoma-Zeiss hæmocytometer counting-chamber.

are ruled on the centre of the disc (*b*). The parallel lines, whether vertical or horizontal, are separated by intervals of $\frac{1}{20}$ mm., and together enclose 400 small squares, the total cross-ruled area being equal to 1 sq. mm. Every fifth small square is ruled horizontally and vertically

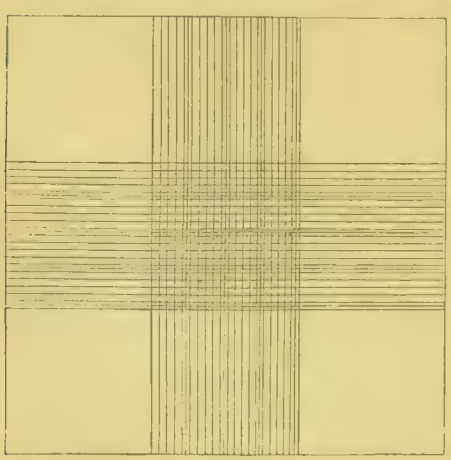


FIG. 58.—Thoma-Zeiss hæmocytometer, ordinary ruling.

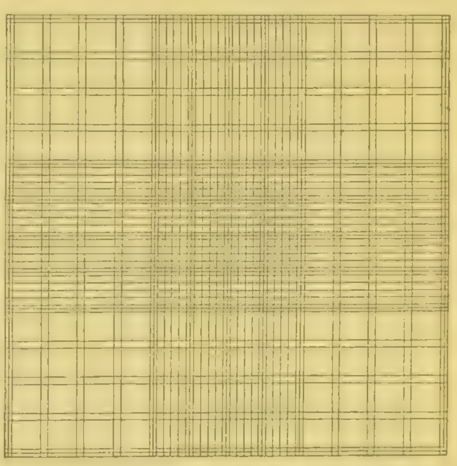


FIG. 59.—Thoma-Zeiss hæmocytometer, Türk's ruling.

with a double bisecting line, and in this way the 400 small squares are marked out into 16 larger squares of 25 each (Fig. 58).

In Zappert's modification of the Thoma-Zeiss instrument the space immediately surrounding the central 400 squares is also cross-ruled so as to form 8 other squares, each equal in area to the 400; these outer

squares are subdivided, not into 400, but into 4. In *Türk's modification* (Fig. 59) these outer squares are subdivided into 16. These modifications of the ordinary ruling can be obtained with the Thoma-Zeiss instrument instead of the ordinary counting-chamber, and are greatly to be preferred for certain purposes, *e.g.* the counting of leucocytes. Slides with Türk's modified ruling are perhaps the most convenient.

Numerous different fluids have been recommended for use in diluting the blood, their exact composition being of no great moment so long as they are isotonic or nearly so. The object is, while diluting the blood, to preserve so far as is possible the cells without change till the examination has been completed. Methyl violet or methylene blue is added in some solutions to aid in distinguishing the leucocytes. The nuclei of the white cells are stained by this means, and the cells thus rendered more easy to distinguish and count.

The formulæ for two of the most commonly used solutions are given below. In Toisson's fluid the methyl violet undoubtedly renders the white cells easier to count, and the glycerin causes them to subside more slowly, which is an advantage in preparing the specimen for counting. On the other hand it serves as a culture medium for yeasts and moulds, besides readily forming precipitates. In Hayem's fluid the cells are better preserved, and multiplication of saprophytic organisms is prevented by the presence of the perchloride of mercury, but for the beginner at any rate the leucocytes are more difficult to distinguish.

Hayem's Solution.

Perchloride of mercury . . .	·5 gramme.
Sodium chloride . . .	1 „
Sodium sulphate . . .	5 grammes.
Distilled water	200 c.c.

Toisson's Solution.

Sodium chloride . . .	1 gramme.
Sodium sulphate . . .	8 grammes.
Methyl violet 5 B . . .	·025 gramme.
Neutral glycerin . . .	30 c.c.
Distilled water . . .	160 c.c.

For counting leucocytes, in low dilutions (1 : 10 or 1 : 20), it is necessary to use as a diluting solution some fluid which will break up the red cells and so render the leucocytes more conspicuous. For this purpose Thoma's solution is convenient.

Thoma's Solution.

Acetic acid . . .	0·3 to 0·5 gramme.
Distilled water . . .	100 c.c.

A small quantity of methyl violet may be added.

The Counting of Red Cells.—All the necessary apparatus should be made ready beforehand. A suitable drop of blood having been obtained in the manner already described, the point of the pipette (A) is placed in it, care being taken to avoid touching the skin of the patient. Gentle suction through the rubber tube is then used to fill the capillary tube up to the mark ·5, or even slightly beyond. It is much more satisfactory to obtain the desired amount exactly, and with practice this can be done almost invariably unless the patient is restive. At the same time great care must be exercised to prevent the admission of any air. If the mark is not hit exactly, the excess may be shaken out by tapping the point of the pipette on a clean cloth gently, or preferably drawing the blood exactly up to the next division, ·6, allowance being made for this in the final calculation. Any blood adhering to the outside of the end of the pipette is carefully removed, and the point plunged carefully into a vessel containing some of the diluting fluid freshly filtered.

Suction must be applied immediately the point of the pipette enters the solution, so that no blood may escape, and must be continued until the fluid reaches the mark 101 above the bulb. The bulb will then contain blood in a dilution of 1 : 200, the capillary portion of the tube, on the other hand, containing diluting fluid only. The ends of the pipette are then closed by a finger and thumb, and the whole shaken so as to thoroughly mix the blood, or the tube may be held horizontally and rotated by holding the two ends between the fingers of either hand. One or two minutes suffices, and then two or three drops of the mixture are blown out to remove the diluting fluid from the capillary portion of the pipette. A drop is next placed on the central disc of the counting-chamber, and at once covered with one of the special cover-glasses supplied. The size of the drop required can only be learnt by experience, but it must be of such a size as to completely or nearly completely cover the disc when the cover has been lowered on to it. If this object is not attained, or if the drop is so large as to run into the moat or across it and under the cover-slip, the slide must be cleaned, dried, and a fresh specimen prepared. The inclusion of air-bubbles also necessitates rejection. If the apparatus is perfectly clean, Newton's rings will appear between the cover-glass and the outer supporting rim of glass either at once or on slight pressure. They are best seen by holding the slide nearly up to the level of the eye. If they fail to appear, the specimen stands condemned. The preparation is allowed to stand for a few minutes to allow the corpuscles to subside; the number of these can then be counted if a rapid survey of the field shows that the corpuscles are evenly distributed.

In place of drawing the blood up to the mark ·5 it may be drawn up to the mark 1, and in this case the dilution will be 1 : 100. The disadvantage of using this lower dilution is that in normal blood, and *a fortiori* in cases of cyanosis, the number of red cells is large enough to cause some difficulty in counting. On the other hand it is the most convenient dilution to use if the red and white cells are to be counted in

one operation, as they may well be in ordinary routine examinations. In oligocythæmia the lower dilution should be used, and in cases of polycythæmia even higher dilutions than 1 : 200 can be made by taking blood up to the mark ·4 or ·3 instead of ·5.

The counting may be made with a Zeiss D or Leitz No. 6, or some objective of similar power. The special cover-slips will not admit of higher powers being used. The examination must be made with a small diaphragm and the concave reflecting mirror.

In dealing with the red cells the number of squares which should be counted varies with the character of the blood under examination. Thoma and Lyon have shown that if more than 1000 cells are counted the instrumental error is usually less than 2 per cent, but that it increases markedly when anything under this figure is taken. A sufficiently large number of squares ought therefore to be counted to include at least this number of corpuscles. In perfectly normal blood, with a dilution 1 : 100, this figure will be reached in counting 80 squares, or with a dilution of 1 : 200 in 160 squares.

The counting should always be conducted on some definite plan. The exact course of procedure is of no great moment, but exactness is ensured by invariably using the same method.

If a start is made from one of the small cells which are doubly ruled both horizontally and vertically (A, Fig. 60), the counting may be conveniently continued in a horizontal direction from left to right of the field, square by square for five squares, *i.e.* up to but *not* including the next square similarly ruled. The process may then be continued in the direction of the arrow, row by row for five rows, *i.e.* up to but not including the next row ruled in the same manner as the first one counted. By this plan the whole area of the ordinary ruling may be counted, and each having a total area equal to 25 small squares in 16 parts all precisely similar. Many other schemes founded on the double ruling of every fifth line suggest themselves as alternatives for the plan suggested.

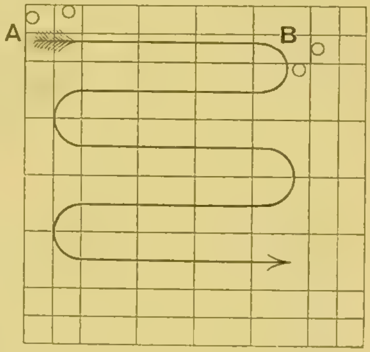


Fig. 60.—Scheme for counting corpuscles.

A certain number of cells will always be found lying to a greater or less extent over the ruled lines, and it is necessary to adopt some plan for dealing with these whereby they are neither omitted altogether nor counted twice. The most usual plan is to count as *inside* a square all those in any way touching the lower and right-hand lines of that square, even though it may barely touch either of them (B, Fig. 60), and as *outside* those touching the upper and left lines, even though they may lie for the most part inside the square (A, Fig. 60). Given the number of small squares counted and the number of red cells found in them, it remains to calculate the total number of corpuscles in a given quantity of

the blood. The total area of the 400 small squares being equal to 1 sq. mm. and the depth of the counting-chamber being $\frac{1}{10}$ mm., the number present in 1 c.mm. will be found if the number of red cells noted is multiplied by the degree of dilution (say 200), by 400, and again by 10, and then divided by the number of squares counted :—

$$\frac{1200\text{ (the number of red cells counted)} \times 200\text{ (the degree of dilution)} \times 400 \times 10}{200\text{ (the number of cells counted)}} = \underset{\substack{\text{The number of}\\ \text{cells in one c.mm}}}{4,800,000.}$$

If all the 400 squares are counted it is sufficient to multiply by 1000 if the dilution used has been 1 : 100, or by 2000 when it has been 1 : 200.

The cleaning of the pipette should be done as soon as the counting is completed. Remove the rubber tubing, shake the pipette, and blow out what remains of the diluted blood with the bellows of a freezing microtome ; then suck up and blow out water, alcohol, and ether in turn. It is best always to suck up the cleansing fluids through the capillary end of the tube, but to blow them out of the other end. In this way the more important measuring portion of the instrument is traversed only by clean liquids. After the cleansing, the inside of the pipette may be dried by passing air from the bellows through it.

If blood clots in the bulb or if the instrument becomes stained it may be more thoroughly cleansed first with acetic acid. The slide should be cleansed by water only, as the cement is soluble in alcohol.

The Counting of Leucocytes.—If an attempt is made to count the white corpuscles in the same preparation as the red, the total number present in the whole of the 400 small squares will, with normal blood and a dilution of 1 : 200, be only three or four. Even with a dilution of 1 : 100 the total number will only reach seven or eight. In either case the number is far too small to justify any conclusion of importance. Many contrivances have been described whereby the area counted may be increased, such as taking the microscope field after its area has been calculated and then counting so many fields. Both the safest and easiest way, however, is to use a counting-chamber in which the area cross-ruled has been extended as in the Zappert or Türk modification (*vide* p. 652). By using either of these instruments the area which can be counted is enlarged nine-fold, and with a dilution of 1 : 100 the number of leucocytes found in a specimen of normal blood will reach sixty or seventy or slightly over, and if two separate drops are examined the total counted will not be far from 150. For all ordinary purposes this figure will give results which are sufficiently accurate, and if the advantages of having only one preparation to make and of being able to count both kinds of corpuscles from the same specimen are taken into account, it is evident that the method has much to recommend it.

When, however, very great accuracy is essential, the use of a specially ruled counting-chamber may be combined with the use of the special leucocyte pipette (with a dilution of 1 : 10) for counting leucocytes ; in this way much larger numbers are obtained, with a proportionate diminution in the error of observation. The use of the "leucocyte pipette" is

in every way similar to that of the other already described. The bore of the pipette, however, is larger, and the accurate measuring of the blood with the subsequent dilution require rather more care and skill owing to the freer flow of fluid. As the dilution is only 1 : 10 or 1 : 20, it is necessary that the diluting fluid should destroy the red cells, otherwise the whites would be obscured by the number of the former. For this purpose Thoma's fluid or some modification of it is commonly used.

Durham's hæmocytometer possesses two great advantages. First, the measuring of the blood is done automatically by a small pipette, and secondly, the pipette can be very easily cleaned. But on the whole it is not to be preferred to the Thoma-Zeiss instrument.

Oliver's method only estimates the red cells, and the errors are very great in cases of severe anæmia.

Daland's Hæmatocrit.—In this instrument, which is a high-speed centrifugal machine, the blood is taken in a capillary pipette and immediately centrifugalised. After this the number of divisions occupied by the red cells is read off on the scale of the graduated pipette, and the number of red cells calculated from that. Each division of the scale contains about 100,000. The result obtained is, of course, an index of the volume of the corpuscles present, and may be used to ascertain this; but except in cases where the reds are known to be normal or nearly so in size, no attempt should be made to use the instrument to calculate numbers.

Histological Examination of the Blood

The histological examination of the blood may be conducted either on fresh films or on films which have been dried and stained. The information which can be obtained does not coincide exactly in the two cases, so that it is often necessary to employ both methods; while on the other hand the object in view may be only attainable by employing one of these two methods, the other being useless. Whichever is employed the first essential is that the slides and cover-glasses be scrupulously clean, otherwise the blood will fail to spread evenly.

In preparing a *wet film* a drop of blood, obtained with the usual precautions, is received on the centre of a cover-glass, and placed as soon as possible, surface downwards, on a slide. If the slide and cover-slip are both clean, the blood will spread itself evenly between them. No pressure must be used to favour the spreading. If prolonged observation be necessary, the preparation should be ringed round with vaseline. The most suitable thickness of the film, and therefore the size of the drop taken, will vary with the object in view. For example, if it is desired to examine the film for malarial parasites the thinnest film obtainable will render the parasites most easily visible, as the red corpuscles will be flat and isolated one from another. On the other hand, the search for filaria is facilitated by a thicker film. A rapid examination with a moderate power will often afford a considerable

amount of information, sometimes sufficing to make a diagnosis, sometimes providing indications for further examination. The points to which observation should be directed as a rule in examination of a fresh film are :—

(*a*) *The Number of Red Cells.*—Unless the variation from the normal is very great it is difficult, if not impossible, to give an opinion on this point, as so much depends on the amount of blood taken and the even spreading of the film ; but taking these circumstances into consideration, any gross change will make itself evident at a glance to a practised observer.

(*b*) *The Shape and Size of the Red Cells.*—In normal blood the shape and size are both very regular ; a very large proportion of all the cells approximate very closely to the standard size, and irregularity of shape occurs only as the result of pressure. Irregularities of size usually occur both in the direction of increase as well as of decrease ; but the change may be chiefly in one direction, *e.g.* increase in the average size of the red cells in pernicious anæmia, or the diminution in chlorosis. Alterations of shape are much better observed in carefully prepared fresh films than in dried, as deformed cells are practically always deficient in the proper degree of elasticity, and any manipulation, such as is necessary in making a dried film, naturally tends to exaggerate the deformities.

(*c*) As the blood is taken the hæmoglobin-percentage may be roughly gauged by the eye, and under the microscope further information may be obtained as to the hæmoglobin-worth of the individual corpuscles. In normal blood the red cells appear as yellow bi-concave discs, the central thinner portion being of a lighter tint. If the hæmoglobin-worth of each corpuscle is high, this central lighter portion can hardly be distinguished ; while, on the other hand, if it is low, the centre of each corpuscle will appear as a relatively large area, almost colourless, and surrounded by a zone containing a small quantity of hæmoglobin, which, by contrast, appears locally increased.

(*d*) As with the red cells so with the white : it is very difficult to appreciate any alteration in the total number unless the variation is considerable ; but a large leucocytosis can easily be recognised, and here assistance is afforded by the fact that a very large proportion of the cells is made up of finely granular "polynuclear" cells—at any rate in the ordinary type of leucocytosis. A careful survey of the whole film is necessary, as the leucocytes are often unevenly distributed. In leukæmia the diagnosis is apparent at a glance from the presence of the enormous increase in the number of white cells. With care even a very large leucocytosis should not be confounded with this condition, the pleomorphism in the myelogenic form and the almost universal lymphocytic nature of the leucocytes in the lymphatic form sufficing to prevent this error.

(*e*) The blood-plates, unless increased in number and searched for at once, usually escape notice, as they become indistinguishable after a few minutes.

(*f*) *Fibrin Formation.*—In very thin films the amount of fibrin found is so small that no deductions can be drawn as to increase or decrease. The films, therefore, should be of moderate thickness, and then the fine strands of fibrin can be seen radiating apparently from blood-platelets. When the amount is increased, the strands are thicker as well as more numerous. Its increase is usually found accompanying leucocytosis in "inflammatory" conditions, but otherwise parallelism is not invariable.

(*g*) For the observation of rouleaux formation, also, a moderately thick film is essential, or the phenomenon will not occur.

(*h*) Blood parasites, especially malarial parasites, filaria sanguinis hominis, as well as the spirochæte of relapsing fever, and trypanosomes can all be found by examining fresh films of blood.

For many purposes fresh films are inadequate, *e.g.* in making differential leucocyte counts, and in many instances in which they may suffice, the same result will be more easily obtained with dried and stained films.

In preparing dried films for staining, either cover-glasses or slides may be used. The writer is convinced that the very best films can be obtained only by means of cover-slips. Apart from questions of technique the slides have, however, the advantages that larger films are secured and that cover-glasses are not required even for examination if an oil immersion lens is used, as the oil may be put directly on the film. Slides are, of course, less liable to break, and may be easily cleaned and used again.

Dry Cover-Glass Films.—The centre of a clean cover-glass is applied to the summit of a drop of blood, care being taken to avoid touching the skin, and the cover-glass is then allowed to fall gently on to a second, in such a fashion that the corners of the two do *not* coincide. The drop must be of medium size. When the blood has spread out, the two cover-glasses are slid apart by pulling on them as exactly as possible in the same plane, and the films are then allowed to dry in the air. This drying may be hastened by holding them, smeared surface upwards, at some distance from the flame of a spirit-lamp or Bunsen burner, not with any intention of "fixing" them at this stage, but because air-dried films, however they are treated subsequently, are, other things being equal, successful in proportion to the rapidity with which they have dried. It is usually recommended that the manipulations should be conducted with the cover-slips held in forceps, as the moisture of the operator's fingers may sometimes cause alterations in the red cells. In practice, if the slips are held by the corners, the writer has found that this seldom occurs, and undoubtedly the cover-slips may be slipped apart more steadily and more truly in one plane by the fingers. This means that better films are obtained. Square $\frac{7}{8}''$ cover-slips are the most convenient size. It is possible by examining a "pair" of cover-slips—that

is to say, any two which have been mutually opposed in spreading a drop—to ensure a complete survey of a sample of blood. By no other method is this possible. The air-dried films, if stored in a pill-box and protected from moisture, may be easily sent to a distance, or they may be kept almost indefinitely, certainly for weeks, and will then stain well and show any structure which is usually demonstrable in films prepared in this manner.

In making films on slides it is necessary to use some device for spreading the blood. The surface of a clean slide near to one end is passed in its short diameter across a large drop of blood. The slide is then placed at rather an acute angle on a second, lying on some firm basis, so that the drop of blood lies in the angle. It is then drawn along the surface of the second from end to end.

The thickness of the film can be regulated by the degree of pressure exercised. Cigarette-paper, gutta-percha tissue, or the needle used in stabbing, may be used for spreading the film. There is always the doubt as to what extent this method of spreading gives a true film, but experience shows that for routine examination the error may be neglected. Average films are more easily obtained by the beginner by this method, and it is certainly to be recommended to the inexperienced for obtaining material for examination, whether such examination is to be conducted by themselves or by others. Once made these films, if properly stored, will keep just as well as the cover-slips.

Fixation.—The dried films before being stained must in most cases be fixed, though in Jenner's method and its modifications the fixation and staining takes place in one operation, and in Gulland's method the films are not even allowed to dry, but are placed wet into the staining fluid. The methods of fixation employed are the application of heat or some chemical substance.

Fixation by Heat.—Films may be fixed by passing them through the flame of a spirit-lamp or Bunsen burner. They should be held in the fingers, as a preventive of overheating, and drawn through the flame quickly, smeared surface upwards, ten or a dozen times. The results are not satisfactory, at least not constantly so, and the method should only be used where heat-fixed films are essential, as in the use of Ehrlich's triacid mixture, and time is limited. The degree of heat and the length of its application are much more accurately and simply regulated by the use of a copper plate.

The plate, which may conveniently measure about 10″ by 4″, is warmed by a small flame placed under one end, and when the temperature of the plate has become constant, its degree at varying distances from the flame may be found by employing as an indicator any fluid such as water, xylol, toluol, etc., the boiling-point of which is known. A drop of fluid placed on the spot heated up to its boiling-point is immediately vaporised. The boiling-point of commercial xylol is about 137° C.; of toluol about 110° C. The degree of fixing necessary varies with the stain which is to be used afterwards, and, within limits, the

amount of time necessary can be regulated by the degree of temperature employed.

The fixation of specimens to be stained with Ehrlich's triacid mixture must be done by heat. It is possible to use this stain after fixation by other methods, as, for example, with a mixture of alcohol and ether, but the results are never so satisfactory. Success in staining with the triacid mixture depends almost entirely on the care with which the antecedent heating has been carried out. If the temperature chosen lies between 110° and 120° C. the heating must be continued for half an hour to an hour. By heating at about 135° C. the time necessary is reduced to ten or fifteen minutes, and at higher temperatures up to 150° C. the time may be further reduced. As in most other things, the method most familiar to the worker produces the best specimens. The writer is accustomed to heat the specimen on a copper plate at about 135° C. for about fifteen minutes.

The copper plate is warmed in the manner above described. The point at which xylol boils on the plate is found, and the films are then placed face downwards, rather to the cooler side of this line, and allowed to remain for ten or fifteen minutes. After removal and cooling they are ready to stain. If it is desired to fix the films at either a higher or lower temperature, all that is necessary is to find the appropriate spot by some indicator with a suitable boiling-point. A few test specimens will soon give the required length of exposure.

Specially made instruments, either hot-air chambers (a hot-air steriliser will do) or Ehrlich's modification of v. Meyer's apparatus, can be procured if greater accuracy is desired, but it is doubtful whether better results are obtained with these than with the simpler apparatus. In staining with Ehrlich's mixture overheating of the films is shown by the red corpuscles taking a pale lemon colour, the definition of the whole specimen at the same time being blurred. On the other hand, in under-heated specimens the red cells take on a dark coppery tint. For staining with eosin and methylene blue a lesser degree of heating is required, and a few minutes at 120° C. or less are sufficient. The same is true for all simple watery stains.

Fixation by Chemical Means.—By absolute alcohol. After drying, the specimens are placed in absolute alcohol for from ten minutes to two hours. They may be left even longer, but the specimens are not then quite so satisfactory.

By ether alcohol (Nikiforoff). This solution, made up of equal parts of the two fluids, is used in the same way as alcohol alone. These two methods are especially suitable in the staining of malarial parasites with eosin and methylene blue. If used before staining with the triacid mixture the specimens must be left in the fluid for the maximum period.

By methyl alcohol. This fluid is the solvent employed for Jenner's and Leishman's stains, and enables a previous fixation to be dispensed with. Its use is unsatisfactory for triacid staining, but excellent for methylene blue and eosin. The specimens are fixed in five minutes.

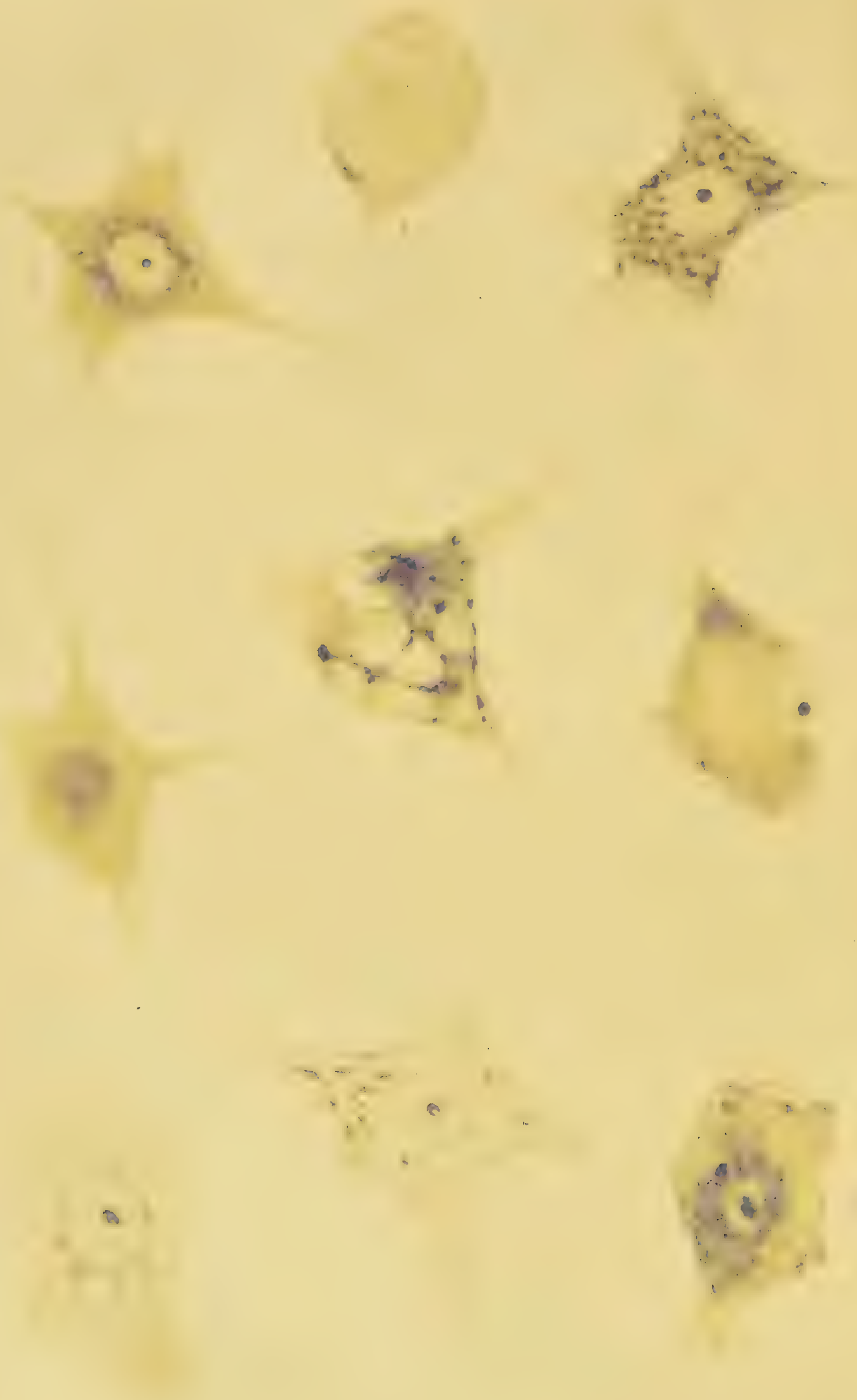
For the examination of the finer structure of nuclei Flemming's strong solution (2 per cent solution of osmic acid 4 parts, 1 per cent solution of chromic acid 15 parts, glacial acetic acid 1 part), applied for ten to fifteen minutes without previous drying, as recommended by Jolly, gives much better results. The specimens must be very thoroughly washed before being stained. Perchloride of mercury, formalin vapour, formalin and alcohol, or the vapour of a 2 per cent solution of osmic acid may be used, but are inferior to one or other of the methods already given.

Staining.—The staining of blood as at present understood dates practically from the introduction by Ehrlich of the aniline dyes for this purpose. He divides these stains into acid and basic dyes. As is well known, these dyes are coal-tar derivates, having a definite chemical composition. Acid stains are those in which the staining agent forms the acid constituent of the salt. Basic stains, on the contrary, are those in which the basic constituent of the salt forms the staining principle. By the combination of certain basic and acid dyes certain new bodies are formed possessing staining properties peculiar to themselves and not present in either of the dyes forming the combination. These Ehrlich calls neutral dyes. The commoner of the acid dyes in use are eosin, orange G, acid fuchsin, and nigrosin, and of the basic, methylene blue, methyl green, gentian violet, and dahlia. In a specimen of blood stained with a simple acid dye certain structures only, such as the eosinophil granules and the red corpuscles, take up the dye, and are therefore called acidophil or oxyphil. On the other hand, when a simple basic dye is used certain other structures, such as the nuclei of the leucocytes, the protoplasm of some of them, take up the stain, and are called basophil. Some structures, however, such as the granules of certain leucocytes, remain unstained whether an acid or a basic dye is used, and being neither basophil nor acidophil, and staining best with "neutral" mixtures, were called by Ehrlich neutrophil. It was shown by Kanthack and Hardy that these neutrophil granules could be stained with acid dyes, at any rate in certain circumstances; and while it is clear that it is not justifiable to conclude that these neutrophil substances are identical in composition, and so in staining reaction, with the oxyphil substances, yet it is clear from the work of Arnold, Pappenheim, Michaelis, and Wölff that the exceedingly rigid laws laid down by Ehrlich as to the staining affinities of the various structures can no longer be upheld. It will be obvious from the above statement that Ehrlich looked upon this interaction between the dyes and certain structures in the various cells as partaking of the nature of a chemical reaction. Thus oxyphil substances, though staining readily with acid dyes, were themselves basic; whilst basophil structures were, on the contrary, themselves acid in reaction.

The method of staining most suitable in any given case naturally varies with the object in view. For ordinary routine examinations, where a differential count of the leucocytes is required, Ehrlich's triacid mixture is, in the writer's opinion, undoubtedly the best.

Ehrlich's Mixture.—Saturated watery solutions are made of orange G,

PLATE VI



Dr. Mott's "Pathology of Nutrition."

PLATE VI.

FIG. 1.—Normal anterior horn-cell (spinal motor neuron), showing axon with cone of origin unstained. Nissl granules in the body of the cell around the nucleus and on the dendrons.

FIG. 2.—Anterior horn-cell from a case of hyperpyrexia. Temp. 108° F. for 36 hours. Diffuse staining of cell, complete disappearance of Nissl granules from the dendrons and periphery of cell.

FIG. 3.—Anterior horn-cell from a case of hyperpyrexia. Temp. over 110° F. Diffuse staining of the whole cell including nucleus, complete disappearance of Nissl granules.

FIG. 4.—Advanced chromatolysis of motor neuron, from the action of the poison of *Bacillus Botulinus.*

FIG. 5.—Advanced chromatolysis of motor neuron, from the action of the poison of *Bacillus Botulinus.* More advanced.

FIG. 6.—Chronic degenerative change of spinal motor neuron, showing vacuolation. General Paralysis.

FIG. 7.—Chronic degenerative change of spinal motor neuron, alcoholic paraplegia. Eccentric position of nucleus, absence of Nissl granules.

FIG. 8.—Chronic degeneration of spinal motor neuron, first dorsal segment of spinal cord in a case of rheumatoid arthritis with disuse-atrophy of small muscles of hand and marked deformity.

FIG. 9.—The last stage of chronic degenerative vacuolation of spinal motor neuron. General Paralysis.

Magnification about 500 diameters.

PLATE VII.

Fig. 1.—Anterior horn-cell. Cajal silver method showing the intracellular fibrillary network.

Fig. 2.—Pyramidal cell of dog after ligation of both carotid, one vertebral and one subclavian arteries. Great swelling of the nucleus, advanced chromatolysis most marked at the periphery of the cell. (Magnification 700 diameters.)

Fig. 3.—Pyramidal cell from cerebral cortex of a dog after ligation of four arteries, showing extreme chromatolysis with commencing extrusion of the nucleus. (Magnification 700 diameters.)

Fig. 4.—Transverse section of a nerve two days after section and before any changes have occurred.

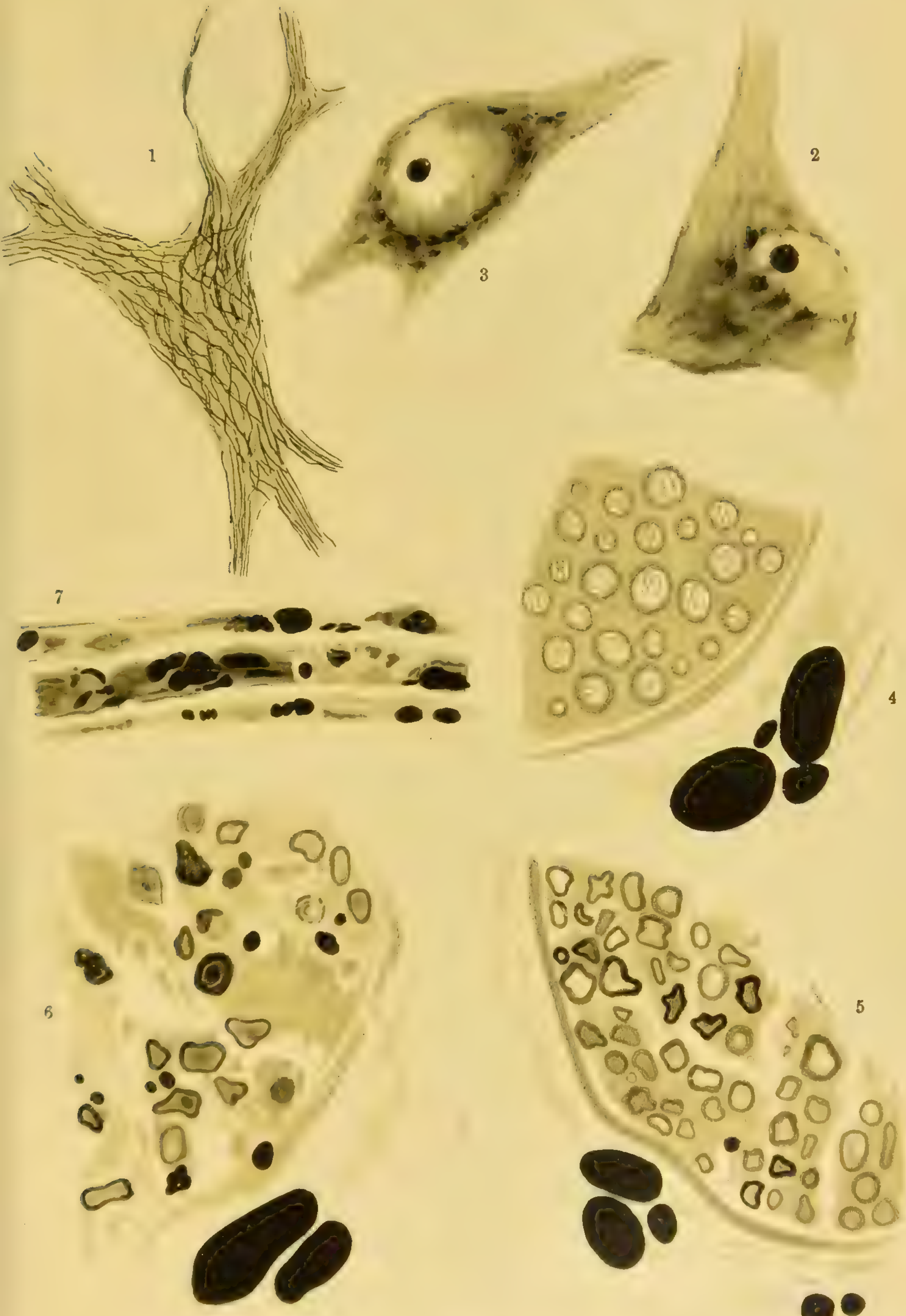
Fig. 5.—Transverse section of a nerve four days after section, showing commencing degeneration.

Fig. 6.—Transverse section of a nerve ten days after section, showing complete degeneration.

Fig. 7.—Longitudinal section of a nerve also ten days after section, showing complete degeneration.

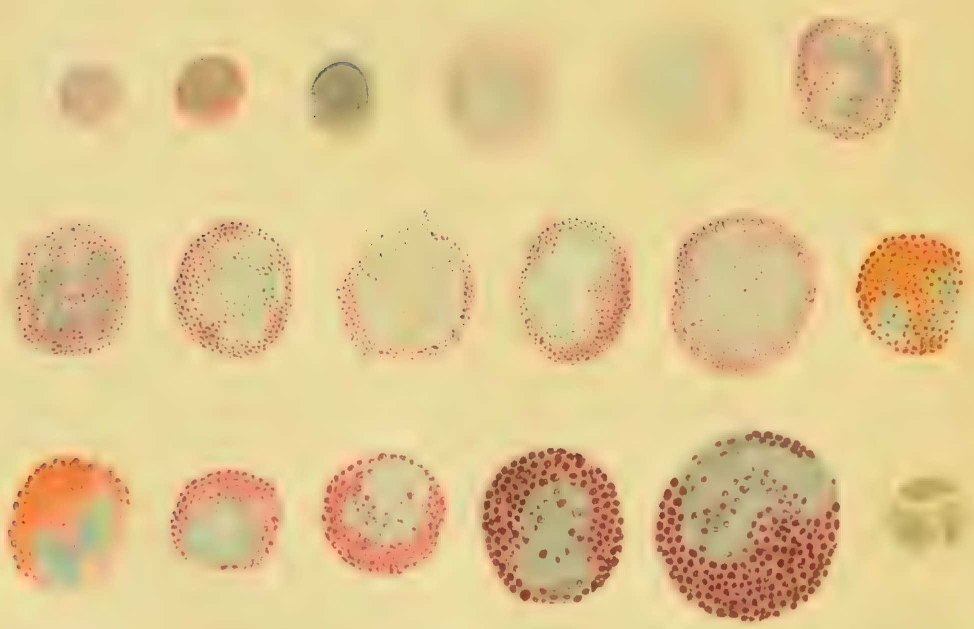
Magnification of 4, 5, and 6, 425 diameters.

Magnification of 7, 600 diameters.

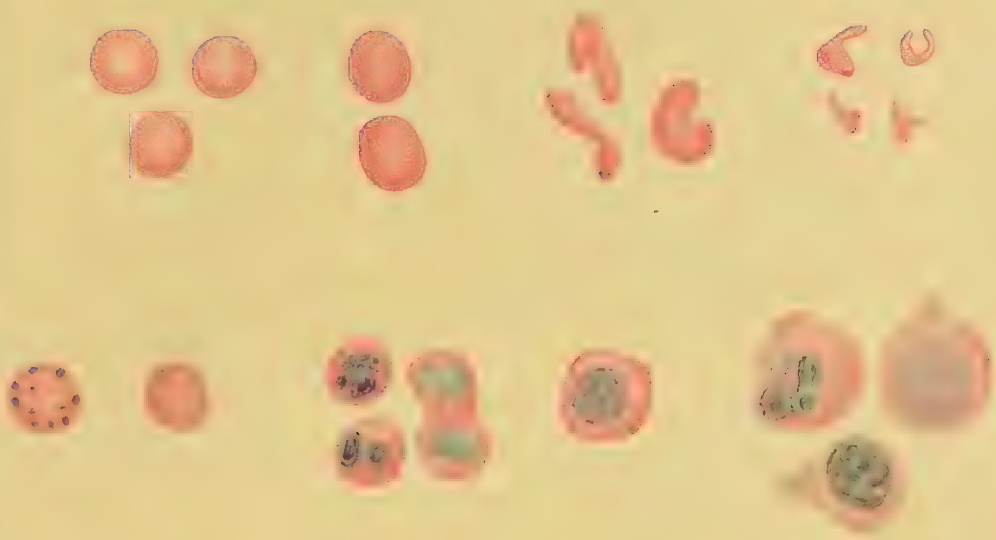


Dr. Mott's "Pathology of Nutrition."

(1) Leucocytes stained with Eosin and Methylene Blue.



(2) A similar set stained with Ehrlich's Triacid Stain.



(1) Normal and abnormal red corpuscles stained with Eosin and Methylene Blue.

(2) A similar set stained with Ehrlich's Triacid Stain.

Drysdale's "The Clinical Examination and Significance of the Blood."

acid fuchsin, and methyl green from chemically pure samples of the dyes, and the solutions allowed to clear by standing for several days. The following mixture is then prepared :—

Orange G saturated watery solution . . .	13-14 c.c.
Acid fuchsin saturated watery solution . .	6-7 ,,
Distilled water	15 ,,
Absolute alcohol	15 ,,
Methyl green saturated watery solution . .	12-5 ,,
Absolute alcohol	10 ,,
Glycerin	10 ,,

The various fluids are measured in the above order, in the same measuring glass. The methyl green should be added in small quantities at a time, with repeated shaking, and when the mixture is complete it should be thoroughly shaken. The mixture is ready for use after standing a few days. It must never be filtered. The stain is very difficult to prepare satisfactorily, and is best bought ready made. Grübler's stain is preferable to any other. To stain a specimen, after it has been properly heated and allowed to cool, cover with a drop or two of the stain and allow it to act for two minutes or more. Overstaining does not occur. The red cells are stained orange or orange-red; the nuclei of the leucocytes bluish green; the eosinophil granules orange-red or copper colour; the neutrophil granules violet. The granules of the mast-cells remain unstained, as do bacteria and malarial parasites. The platelets take on a mauve colour. The protoplasm of the lymphocytes is faintly stained a pinkish or greyish colour.

Eosin and Methylene Blue Stain.—The use of eosin and methylene blue consecutively is followed by such inconstant results that the method is gradually going out of use. The specimens to be stained in this way may be fixed with alcohol for fifteen minutes, methyl alcohol five minutes, or by heat at 120° C. for a few minutes. To stain, place them in 0·5 per cent solution of eosin, in 70 per cent alcohol, for three or four minutes, wash and dry. Next place the specimen for half a minute in a concentrated watery solution of methylene blue, wash, dry with blotting-paper, and mount in balsam. If the specimen is successful, the nuclei of all the leucocytes appear blue; the red cells, eosinophil and neutrophil granules red, and the protoplasm of the lymphocytes various depths of blue. The mast-cell granules remain for the most part unstained. Platelets and malarial parasites take on a pale blue. In many cases the neutrophil granules are not differentiated, a diffuse red stain marking the situation of the protoplasm; sometimes even this degree of staining is not attained, and the polymorphous nuclei are seen surrounded by a colourless ring.

Staining with Eosin and Methylene Blue Compounds.—This method, introduced by the late Dr. Louis Jenner, has been improved upon by Professor Leishman, who has applied it to the Romanowsky method; and

with this modification of Jenner's stain, specimens may be obtained in many cases equal to the best Romanowsky staining.

Leishman's Stain.—Two solutions are made—(*a*) A 1 per cent solution of medicinal methylene blue in distilled water, to which is added a 0·5 per cent of sodium carbonate to make it alkaline. The solution is heated at 65° C. for twelve hours, and then allowed to stand for ten days. (*b*) A 1-1000 solution in distilled water of eosin BA extra. An equal volume of this is added to solution (*a*) in a large open vessel, and the mixture allowed to stand for six to twelve hours. From time to time it must be stirred. The precipitate which forms is collected on a filter and washed till the washings are nearly colourless. It is then collected, dried, and powdered. For use a 1·5 per cent solution in methyl alcohol is prepared. Without any preliminary fixing, three or four drops of the stain are placed on the specimen, which is held in forceps and rocked to and fro. No attempt is made to prevent evaporation. At the end of half a minute to a minute six or eight drops of distilled water are added (twice as much water as stain), and the diluted stain, on the surface of which a metallic shimmer appears, is allowed to act for five minutes. The specimen is gently washed with water and placed in distilled water for about one minute to differentiate, dried with blotting-paper, and mounted. The red cells and the eosinophil granules are stained pink; the nuclei of the leucocytes varying depths of purplish red according to the density of their chromatin; the neutrophil granules red; the protoplasm of the lymphocytes bluish, with here and there purple granules; mast-cell granules deep violet; blood-plates purple red in the centre, with pale blue margin. The method is an exceedingly simple one, and gives excellent results as regards all the different blood-cells. Its weak point is in the occasional partial failure in the staining of neutrophil granules. For the demonstration of malarial parasites or trypanosomes it is particularly well adapted.

Romanowsky-Ziemann Method.—In this method, of which there are many modifications, the eosin and methylene blue solutions are mixed at the time of staining, a precipitate forms, but this condition, so far from diminishing the perfectness of the staining, is essential to its success. The solutions used may be those employed in the manufacture of Leishman's stain (*v. supra*). Four parts of the eosin solution are mixed with one part of the methylene blue, and allowed to act on the specimen for five minutes, which is then washed in water, dried between blotting-paper, and mounted. For staining malarial parasites, or demonstrating the granules present in certain lymphocytes, this method is unsurpassed. The specimen should be fixed in alcohol or methyl alcohol.

Staining of Mast-Cells.—The granules of these cells stain exceedingly well either by Leishman or Romanowsky method. They are very readily soluble in water, and do not stain by Ehrlich's stain. Thionin or toluydene blue in 60 per cent alcohol stains them exceedingly well.

Examination of Dry Films.—Many of the finer histological details of the blood, to be described later, which are not distinguishable in wet films,

are readily made out by the examination of dry ones. One of the chief uses to which this form of preparation is put is the making of differential counts of the red and white cells of the blood. The best and by far the easiest way to do this is by using a mechanical stage. The film selected for counting must be properly spread and perfect, or nearly so, in its staining. By means of the moving stage successive portions of the film are in turn brought into the field, and the various forms of leucocytes and any abnormal red cells are noted, care being taken not to go over the same ground twice. When the number of leucocytes counted has reached the required number (500 cells is enough for ordinary purposes, though 1000 is much better) the percentage of the various forms is calculated. From this percentage, if the number of leucocytes per c.mm. has been estimated, can be calculated in turn the absolute numbers of each variety of leucocyte per c.mm. of blood. The number of nucleated reds may also be roughly arrived at. If in counting 1000 white cells 100 nucleated red have been encountered, and if the total number of leucocytes in the specimen of blood equal 20,000 per c.mm., then it follows that there will be approximately 2000 nucleated red cells in the same volume. Large and small nucleated reds, called respectively megaloblasts and normoblasts, should be estimated separately, as their significance is not always the same.

The Red Cells

Seat of Origin of the Red Cells.—It is generally accepted that in extra-uterine life in health the red cells are exclusively formed in the red marrow. The non-nucleated cell of the circulating blood may be traced back to the nucleated red of the erythroblastic tissue in the bone-marrow. How much further back it may be traced is still a matter of opinion. The present tendency (Müller, Wölff, Pappenheim, and others), however, is to believe that it arises, in common with the leucocytes, from a primitive cell somewhat resembling a lymphocyte. The cell is large, contains no hæmoglobin, and possesses an oval or rounded faintly staining nucleus. From this cell, by a process of mitotic division and differentiation along several lines, the red cells, lymphocytes, and the granular cells gradually develop by stages. The stage in the erythroblast series immediately preceding the normoblast is the megaloblast. Others believe that the primitive red and white cells are distinct. Under pathological conditions the mode of formation of red cells may revert gradually to the embryonal type. The red marrow, which in the adult is considerably restricted in area, spreads to the limits which are observed in early childhood, and the spleen and liver may once more take on the function of erythrocyte formation which they possess in fœtal life ("Myeloid transformation"). Hayem's view, which has received but little support, is that the red cells are developed from the blood-platelets. How exactly the nucleated red cells become transformed into the non-nucleated erythrocyte is not certain. Pappenheim, Neumann, and others hold that the nucleus

gradually disappears inside the cell; on the other hand, Rindfleisch and Muir maintain that the nucleus is extruded. The tendency is rather to accept the former view; among other arguments used in support of it being the appearance found in some of the cells with basophilic granular degeneration of the protoplasm, which is looked upon as a sign of nuclear destruction.

The Number of Red Cells.—Till some method, at once accurate and easy of application, is available for estimating the total volume of the circulating blood, there can be no reliable enumeration of the absolute number of red cells in the body. At present our attempts are directed to ascertaining as far as is possible the number present in a given standard unit volume. This unit, for practical purposes, is 1 c.mm., and in this volume there are, roughly speaking, 5,000,000 red cells in the healthy man and about half a million less in woman. These figures are, in round numbers, those first obtained by Vierordt and Welcker, but by most later observers they are put rather higher, and in robust young males it is common to find counts of 5,500,000. Cohnstein and Zuntz have shown that the blood in the large veins and arteries has an equal number of corpuscles, but in the capillaries it may vary in this respect, though the blood may show no other change. This can be seen in congestion from local causes. In new-born infants the numbers are much increased, and, as a rule, reach 5,500,000, but may be six or even eight million. As soon as the infant is fed, however, this increase begins to diminish, rapidly disappears, and at the end of ten days or a fortnight the adult standard is reached. The difference in numbers between the two sexes does not make its appearance before the age of puberty in the female. Under certain conditions both in health and disease the normal numbers undergo considerable variations.

Factors which raise the Number of Red Cells in a given Volume of Blood.—High Altitudes.—It was observed, first by Viault and subsequently confirmed by Köppe, Egger, and others, that removal from the sea-level to high altitudes is followed within a few hours by an increase in the number of red cells, which reaches a maximum at the end of two or three weeks, the increase varying directly with the altitude attained. On returning to a lower level the increase rapidly disappears again. At first the increase is due apparently to the presence of a number of small, ill-shaped cells, and at this stage it is not accompanied by any increase of the hæmoglobin or of the total volume of cells (Köppe). Later the microcytes and poikilocytes disappear, and are replaced by normal red cells, a rise in the amount of hæmoglobin taking place at the same time. The increase takes place even in balloon ascents (Jolly), and it is difficult to imagine a real increase in this circumstance, though Gaule has observed nucleated red cells. The explanation of these facts is still very obscure. Viault was of the opinion that the increase was only relative, and due to a concentration of the blood caused by the dryness of the atmosphere. Schumburg and Zuntz, whilst agreeing that the increase was relative, ascribed it to altered distribution of the corpuscles in the vessels. On

the other hand, Köppe's observations point strongly to an increased formation of red cells, called for by the diminished supply of oxygen at the higher altitudes. Reasons may be urged against the acceptance of any of these views as accounting singly for all the observed facts, but they nevertheless must all be admitted as explaining in part the changes found. It is probable, or at least possible, that some at present unknown factors are at work in addition. The blood of natives of high altitudes present the same features, though in a lesser degree, as that of recent arrivals.

In cyanosis accompanying general venous engorgement, as in valvular disease of the heart with failing compensation, or more markedly still in congenital heart disease, the red count is raised. This is probably due to alterations in the circulation, whereby the red cells accumulate to some extent in the peripheral vessels. Counts of 7,000,000 are not uncommon, and I have found over 10,000,000 in pulmonary stenosis. This form of polycythæmia is also seen in certain cases of enlarged spleen with cyanosis.

In cases where from one cause or other there is a large quantity of fluid withdrawn from the blood, a high degree of polycythæmia may appear. In cholera or other conditions accompanied by copious watery discharge, with profuse sweating or incessant vomiting, in conditions where fluid effusions rapidly reaccumulate, as after paracentesis, in any circumstances in fact where the abstraction of fluid is large and sufficiently rapid to prevent for a time the normal readjustment, the red count may rise to six or seven million or even higher. Deprivation of fluid which raises the count acts, of course, in the same way.

In poisoning by phosphorus or by coal-gas, polycythæmia, sometimes of high degree, occurs. In phosphorus poisoning it makes its appearance when the vomiting becomes pronounced, and is probably to be explained, at least in part, by this circumstance. In coal-gas poisoning the result is probably due to the action of the carbon monoxide contained in it.

Oligocythæmia is found in many conditions. It occurs after hæmorrhages, is common in many cachexias and toxic conditions, and may follow or accompany acute or chronic infections. Dilution of the blood, increased destruction or loss, and diminished formation underlie this condition, and in many cases more than one of these factors is probably at work. The diminution of the red cells after meals, which is most marked about the same time that the leucocyte count reaches its height, is due probably to dilution. It is certain at any rate that ingestion of fluid, whether by the mouth or in any other way, temporarily reduces the red count.

Alterations in Size of the Red Cells.—The average diameter of the red corpuscles is about 7·5 μ. The size will vary to some extent according as the cells are measured in a wet or a dry film, while the thickness of the dry film will have some influence, the cells in thin films being always more flattened or spread out than in thick ones. In normal blood, though there are occasionally cells varying 1 or 1·5 μ on either side of the mean, the very great majority of the cells differ very slightly from the

average in size. In *pernicious anæmia* the average size is increased to a degree that is easily appreciated by the practised eye, and is readily demonstrated by comparison with a normal film. The most striking feature, however, in this condition in regard to size is the very great variation. In any one field there are very few cells exactly alike. Large red corpuscles, attaining sometimes twice the diameter of normal cells, are common, as are small cells down to those whose diameter is hardly half that of the average. The larger cells are called megalocytes, the smaller ones microcytes. Megalocytes, common in pernicious anæmia, are not common in other anæmias, unless it be in infants in the condition known as anæmia pseudoleukæmica infantum. They may exist, if only in a small proportion, in any severe anæmia. In pernicious anæmia, however, they are rich in hæmoglobin, while in secondary anæmias the hæmoglobin-content is low. In chlorosis the red corpuscles, except on the rare occasions when a considerable oligocythæmia is present, are much more regular, but the average size is smaller than natural without coming within the definition of microcytes. In secondary anæmias the red cells are not markedly altered in size, unless the anæmia be extreme in degree, and then the variations in size may approach those seen in the pernicious type.

Alteration in Shape, or Poikilocytosis, is not peculiar to any one variety, but may be seen in any form of severe anæmia. It is, however, most commonly seen under conditions in which variations in size are present, and for that reason is most marked in pernicious anæmia. Many of the poikilocytes are quite small, and are regarded by Ehrlich as arising by fragmentation of the larger forms in order to afford a greater respiratory surface. These deformed corpuscles are deficient in the normal elasticity, and many of the poikilocytes seen in dried and stained specimens of blood are exaggerations caused by manipulation in preparing the specimens.

Variations in Volume of the Red Corpuscles.—The total volume of red corpuscles in a given measured quantity of blood may be estimated either by sedimentation or by centrifugalising. In both these methods the results are only approximate. If the attempt be made to estimate the average volume of the individual corpuscle, one of these methods must be used in combination with a count. As von Limbeck pointed out, this is multiplying error by combining two methods, neither of which is exact. Clinically, at any rate, the knowledge of this volume of the individual corpuscle is of no value, but the total volume in a measured quantity has been used as a means of estimating their numbers. It is obvious, however, apart from any technical drawbacks in the methods, that when the individual cells vary greatly in size such estimations must be quite unreliable. By estimating the volume of the red cells the extent of the respiratory surface available may be gauged, but this important inference is elicited probably quite as accurately by the counting and microscopical examination which is essential in all severe anæmias.

Variations in Staining Reactions.—Living red cells do not take up any

stain, but after death they show a particular affinity for acid dyes, especially eosin; though they will stain to some extent with almost any dye. In contact with a mixture of an acid and a basic dye, as for instance methylene blue and eosin, they select the acid dye exclusively. In certain cachexias and severe anæmias this selective affinity is, in some degree lost, and they take on a colour intermediate to the two dyes, but inclining sometimes to the one, sometimes to the other. All the cells do not show the change. To this change Ehrlich gave the name of anæmic degeneration, but it is now more commonly called polychromatophilia, the term first used by Gabritschewsky. As to its significance opinions still differ. Ehrlich's view is that it is an expression of degeneration in dying cells which are losing their hæmoglobin and acquiring basophilic properties owing to coagulation-necrosis, with absorption of the proteids of the blood. He says many of the cells showing this change are irregular in shape, with frayed margins, as if on the point of dissolution. After hæmorrhages such cells may be found within the first twenty-four hours, before there are any signs of regeneration, such as the presence of nucleated reds, and they appear in conditions of malnutrition, notably in animal experiments, where blood regeneration could hardly be expected. The change, too, is much more marked in the large nucleated red cells than in the normoblasts, which are the typical cells of normal regeneration. Maragliano's researches led him to the same conclusion. On the other hand, Gabritschewsky, Askanazy, and others are of the opinion that cells showing these changes are not degenerating but young cells. They point to the presence of these changes in normoblasts of normal structure, even in those undergoing karyokinesis, and in normal fœtal marrow. So far as obviously degenerating cells go, Ehrlich's view is generally accepted; but for other cells the majority hold that the changes are to be regarded as not in any sense degenerative, but as an expression of youth and due to a deficiency of hæmoglobin or imperfect differentiation.

Granular Basophilia (Degeneration) of the Red Cells.—This condition makes its appearance in the blood in most, if not in all, forms of anæmia, and in many toxic and infective processes. In simple staining with methylene blue, or with methylene blue and eosin, some of the cells are seen to contain granules deeply stained with the basic dye. Sometimes the granules are very fine, and thickly set throughout the substance of the cell; sometimes they are coarse, or one cell may contain granules of varying size. The coarse granules are, as a rule, not so numerous. The cells containing them may be either nucleated or non-nucleated, and the protoplasm may show either the normal staining reaction or polychromatophilia. Lazarus regards them as products of nuclear destruction, and Grawitz as due to degeneration of the protoplasm, caused by some circulating poison. From the results of experimental lead poisoning, Sabrazes regards them as evidence of active *regeneration*, and believes their disappearance indicates the failure of the bone-marrow. Lutoslewski (quoted by Türk) has recently come to the same conclusions,

after repeating and extending Sabrazes' experiments. That they occur in healthy animals after hæmorrhage supports this opinion. Whatever their nature or significance, their diagnostic or prognostic value appears very limited, unless it be in lead poisoning, where they are found in the absence of symptoms of this condition, and it is said of anæmia also.

The appearance of Nucleated Red Cells in the Peripheral Blood.—Though nucleated red cells may be found in small numbers in the blood of infants for a few days after birth, it may be stated generally that they do not appear in the blood under normal conditions during extra-uterine life. When they occur they vary greatly in size, and are usually classified as megaloblasts, normoblasts, and microblasts. *Normoblasts* are cells of the average size, and contain, often rather to one side, a small deeply-staining nucleus, rounded in shape and well defined. Occasionally the nucleus is divided into two or three lobes, united by connecting strands; or occasionally two or three separate nuclei are present. The protoplasm usually stains in a normal manner. *Megaloblasts* are large cells, sometimes reaching three times the size of a normoblast. The nucleus, as a rule, stains rather faintly, and is not only larger, but fills a larger proportion of the cell than does that of the normoblast. The protoplasm of the cell often shows polychromatophilia, and in dried films is much more often frayed at the circumference than are the normoblasts. *Microblasts* are nucleated cells, smaller than normoblasts. With a nucleus resembling that of the normoblast, they are surrounded by a thin ring of protoplasm which is usually ragged. Their significance is unknown. The normoblast is properly found in the erythroblastic tissue of the bone-marrow, and is by common consent the parent of the normal red cell of the blood. It is regarded, therefore, when it appears in that fluid, as a sign of activity of the bone-marrow, and to that extent is a favourable sign in anæmia. It is found in both forms of leukæmia, in much larger numbers in the myelogenic form, in pernicious anæmia, after hæmorrhage, and in many secondary anæmias, notably in certain intoxications in which blood destruction is followed by attempts at repairing the loss.

The megaloblast is not found normally in the body anywhere after birth, and its appearance therefore denotes a reversion, on the part of the erythroblastic tissue of the bone-marrow, to a fœtal type. It is found most commonly in anæmia of the pernicious type, which may be secondary, as in bothriocephalus anæmia, or primary. In anæmia pseudoleukæmica infantum, too, they sometimes are present in large numbers, and not infrequently form a majority of the nucleated red cells in the blood in this disease. They are present, too, in leukæmia, and occasionally in other very severe anæmias. They are associated always with normoblasts.

Variations in the Hæmoglobin-Content of Red Cells.—The amount of hæmoglobin in a given volume of blood is usually expressed as a percentage of the normal. To obtain the hæmoglobin-worth or colour-index of the individual corpuscle the percentage of the normal of hæmoglobin is divided by the percentage of the red cells, and if both percentages are normal the colour-index will equal 1. It is theoretically

possible if any alteration take place either in the direction of increase or decrease that the hæmoglobin and corpuscles will vary in exact proportion, but practically such is never the case. In pernicious anæmia, where the cells may fall to 20 per cent of the normal, the hæmoglobin may not fall in the same case below 25 or 30 per cent, so that the colour-index will be high—

$$\frac{30 \text{ per cent hæmoglobin}}{20 \text{ per cent corpuscles}} = 1{\cdot}5 \text{ C.I.}$$

In this disease the colour-index is nearly always higher than 1, though in remissions it may fall below that figure. In chlorosis, on the other hand, the loss of hæmoglobin is out of all proportion to the loss of cells, and the colour-index may fall to ·5 or ·3, or even lower. In secondary anæmias of the ordinary type the results lie, as a rule, between these extremes, ·7 or ·8 being a common figure. In examining a dried and stained specimen of blood, it is possible to appreciate these differences. In films of equal thickness, cells of blood of the chlorotic type show a much larger proportion of their central area unstained or faintly stained. In blood of the pernicious type, on the other hand, the central lighter area may be absent, or only slightly marked in proportion to the larger size of the cells in that condition.

Blood-Platelets.—In specimens of fresh blood these bodies soon disappear, but in fixed and stained specimens they may be seen lying nearly always in clumps, and with ordinary stains taking on a faint colour. Their precise nature is still in doubt, as is the question whether they exist as preformed elements in the blood. Recent researches (Maximow and others) point to their being formed from the breaking down of red cells. Their numeration is not easy, and the results obtained in normal blood vary within very wide limits—200,000 to half a million or more. For practical purposes an increase or decrease may be gauged by the appearance of the stained film. In leukæmia, in severe secondary anæmia, and especially in chlorosis they are increased. On the other hand, in purpura, hæmophilia, and pernicious anæmia they are decreased.

Bremer's Reaction in Diabetic Blood.—His earlier methods having proved unsatisfactory, Bremer has modified his test and now advises that it should be performed as follows: Thick films on glass slides are made of diabetic blood and also of some control blood. The films are gradually heated up to 135° C. in the course of eight to ten minutes. After cooling, they are placed for two to five minutes in a 1 per cent solution of Congo red, methyl (not methylene) blue, or Biebrich scarlet. They are then rinsed in distilled water and dried. Congo red and methyl blue stain normal but not diabetic blood; while Biebrich scarlet stains diabetic but not normal blood. Freshly prepared solutions of the stain are essential. The reaction is said to occur before sugar appears in the urine, and also during its temporary absence under treatment. The reaction has been confirmed by many authors, notably Legoff, who states that it is probably due to the presence of glucose. The reaction has

been found in some cases of leukæmia, in Graves' disease, and in lymphadenoma.

The Iodine Reaction or Iodophilia.—If a film of normal blood be exposed to the action of iodine, the red corpuscles are stained yellow, as are the leucocytes, though rather more faintly. The various leucocytes can be distinguished from each other by their nuclei, which are sufficiently differentiated from the protoplasm. Under certain pathological conditions a varying number of the polymorphonuclear cells show in their substance brown granules. This is the iodine or glycogen reaction, which is never manifested by the eosinophils and lymphocytes. The granules may be fine or coarse, or a diffuse brown discoloration of the protoplasm may be seen instead of them. The brown granules are sometimes extra-cellular, and were originally described by Gabritschewsky as occurring in the blood—Locke, Gulland, and Kaminer among others have defined the circumstances in which the reaction appears there. The majority of the conditions in which it is found would fall into the class accompanied by inflammatory leucocytosis, and especially those which are associated with suppuration. Locke has shown that iodophilia, without leucocytosis, may be present in gangrenous appendicitis. It is found also in severe anæmias, and various toxic conditions such as uræmia. Its value lies in confirming the presence of one of these conditions. In the writer's opinion, a very considerable experience is necessary before giving an opinion as to the presence of the reaction unless it is well marked. The substance which gives the reaction is glycogen or some nearly allied body.

The method of performing the test is exceedingly simple. A thin film of blood is allowed to dry, and placed face downwards on a drop of the iodine solution and examined.

Iodine	1 part.
Iodide of potassium	3 parts.
Distilled water . . .	100 parts.
Gum arabic	in excess.

Ehrlich recommends the exposure of the film to iodine vapour in a closed vessel containing iodine crystals.

The Leucocytes

Origin and Development of the Leucocyte.—After it had been established by the observations of Wharton Jones and Max Schultze that the colourless corpuscles in the circulating blood are not all of the same kind, their place of origin and mode of development naturally assumed a greater importance. It was suggested by Virchow that the small lymphocytes arose in the lymphatic glands and the large mononuclear cells in the spleen, and that once having made their way into the circulation they there underwent a gradual transformation into the different types found circulating in the blood. This hypothesis predominated up to the

time of Ehrlich, and with certain important modifications has held its ground more or less successfully as one of the accepted explanations of leucocyte formation. Uskow and his pupils may perhaps be regarded as the most thorough-going advocates of this view in more recent times. Uskow holds that the small lymphocyte is the youngest of the leucocytes, and has its origin in the lymphatic glands, spleen, and the lymphatic tissue of the bone-marrow. After entering the circulation it enlarges to form the large lymphocyte. These two cells, the small and large lymphocytes, are the young cells. The large lymphocyte in turn further enlarges, and the nucleus becomes indented or kidney-shaped to form the large mononuclears and transitionals. These are the adult cells. In the next stage the nucleus becomes polymorphous and richer in chromatin. The protoplasm loses its basophil character and develops fine granules, which are neutrophil in character. These are the ripe or old cells. According to some authors the eosinophils are developed from the neutrophils by increase in size of the granules and their acquirement of a greater affinity for acid stains. These would form over-ripe cells. Mast-cells are not taken into consideration. The direct demonstration of the phases of development in the blood is wanting; it is assumed, therefore—although some of the transitions may, and in fact do, occur there—that for the most part these changes take place during a period of retirement in the blood-forming organs.

Ehrlich and his followers hold, on the other hand, that the morphological differences in the various leucocytes are proof of separate seats of origin, and not of progressive ripening of a single cell. The granule-free cells, that is to say, the small and large lymphocytes, he regards as arising exclusively from lymphoid tissue, which he does not recognise as having any place in the bone-marrow. The granule-bearing cells of the blood, on the other hand, whether neutrophil, eosinophil, or basophil, are formed exclusively in the bone-marrow, and have their origin in cells which differ from them only in having simple, round, or oval nuclei as compared with the polymorphous character of the nuclei of their descendants. The spleen plays only a subordinate part, and gives rise to certain cells—the large mononuclears—which may, however, also arise from the bone-marrow. These cells may develop in the circulation into polymorphonuclears (neutrophils). The different varieties of granules, the study of which was so greatly stimulated by his researches with aniline dyes, Ehrlich holds to be special metabolic products of cellular activity, and to be specific for each cell. The different leucocytes contain granules differing in size, in staining reaction, and in solubility; any given variety contains only one kind of granule, and transitions from one variety to another never occur. Furthermore, he denies to the lymphocytes the possession of any power of spontaneous movement, so that while the granule-bearing cells "wander" actively, as a result of chemical stimuli, the lymphocyte is limited, so far as alteration of position is concerned, to a purely passive part. Ehrlich's conception has been attacked from all sides, and it must be admitted that on many points his original thesis cannot be sustained.

Wölff and Hirschfeld have shown that lymphocytes possess the power of amœboid movement. Michaelis and Wölff have been able to demonstrate, by means of Romanowsky's stain, the presence of purple granules in certain of the lymphocytes. On these two grounds chiefly, Wölff holds that Ehrlich's distinction between granule-free and granule-bearing cells breaks down. These granules, which can also be demonstrated by Leishman's or Wright's stains, are very inconstant in number, size, and distribution throughout the cell; and it is by no means certain that they are granules in Ehrlich's sense. The problem, however, which has given rise to the greatest controversy is that of the seat of origin of the different varieties of leucocytes. A multitude of papers has been published by Saxer, Pappenheim, Wölff, Gulland, Grawitz, and others, differing in many points from each other—sometimes in essentials, sometimes in names only, but agreeing more or less in the fundamental point that all leucocytes, and some say red cells as well, arise from a single undifferentiated cell, resembling in many respects the lymphocyte. Pappenheim regards all cells with rounded nuclei and basophil granule-free protoplasm as lymphocytes, and holds that both the red cells and leucocytes are derived from a basophil marrow-cell resembling the lymphocyte of the blood. This earliest least differentiated cell is larger than the small lymphocyte, contains a faintly staining (amblychromatic) nucleus, and by mitosis gives rise to a more highly differentiated cell with a nucleus which stains more deeply (trachychromatic). The stress he lays on the pale staining nucleus as an expression of youth, compels him to assert that the polymorphonuclear cells of the blood are derived immediately, not from the myelocytes of Ehrlich, which have round faintly-staining nuclei, but from small deeply-staining mononuclear cells with neutrophil granules, which he finds in the marrow and calls pseudolymphocytes. Ehrlich's myelocyte he regards as one of several intermediate stages in the differentiation of this type of cell from the original "lymphocyte." In like manner, by a gradual process of division with differentiation, all the other varieties of cells are evolved from the original cell. So, too, with the red cells. The undifferentiated lymphocyte divides by mitosis, giving rise to megaloblasts; from the megaloblast arises in turn the normoblast. These changes can be traced in adult as well as in fœtal marrow. The primitive cell can be found also in the lymphoid tissue and the spleen. When, however, a cell has once been differentiated, it remains true to its type, and transitional forms never occur. Wölff calls the primitive leucocyte the "indifferent myeloid cell," but in contradistinction to Pappenheim would separate it strictly from the lymphocytes. He agrees that from this cell all the various types of leucocytes, as well as the red cells, are developed. In post-embryonic life the bone-marrow furnishes the granule-bearing cells, the lymph-glands the lymphocytes, and the spleen the large mononuclears; but in each of these situations indifferent lymphoid cells are to be found, so that under certain conditions a myeloid transformation of the blood-forming organs may take place. Dominici supports Pappenheim, as does Nägeli, except that he would distinguish

in the marrow a granule-free cell with certain differences from the ordinary lymphocyte, which he proposes to call the myeloblast, believing it to be an early stage in the development of the myelocyte. Taylor, Ribbert, Muir, and others follow Ehrlich. It is impossible here to enter fully into the maze of contradictory hypotheses, nor is it from the clinical point of view of immediate importance. Most of these investigations, it must be remembered, have been embryological, and the mode of primitive blood-formation differs widely from that obtaining in post-embryonic life. It may be said that the majority of these investigators are agreed that all the leucocytes, and probably also the red cells, arise from a single primitive cell by a gradual process of differentiation along different lines; on the other hand, most observers, especially those most exclusively engaged in clinical work, would agree that in post-natal life no transformation of established forms occurs. As to the precise steps in the evolution of each cell, the extent to which the fœtal scheme persists in after-life, or the degree in which, under pathological conditions, the adult scheme may revert to an earlier type, the recent tendency is, on the whole, to admit of a greater latitude of opinion than formerly.

Leucocytes.—The first attempt to distinguish between the different forms of leucocytes was made by Wharton Jones, who divided the white cells into those which were granular and those which were non-granular; and the former, again, into those containing fine and those containing coarse granules. Max Schultze was able to distinguish four forms: (1) Small round cells possessed of a round nucleus surrounded by a small amount of non-granular protoplasm; (2) larger cells also with a round nucleus, but surrounded by a large amount of non-granular protoplasm; (3) cells containing more than one nucleus embedded in a finely granular protoplasm; (4) cells containing coarse granules.

These cells may be readily recognised in any examination of a fresh specimen of blood, but for their further and easier differentiation we are indebted to the researches of Ehrlich on the staining reactions of the different cells to various aniline dyes. Ehrlich saw in these various reactions an expression of a chemical interaction between the dye on the one hand and the different components of the various cells on the other. Employing these methods he was able to distinguish the following forms:—

(1) *The Lymphocytes* are the smallest of the white cells, and are somewhat arbitrarily divided, according to their size, into the small and large lymphocytes. As a class they vary in diameter from that of a red cell, or rather less, to about one-third more, or from 6 μ to 10 μ. The protoplasm and the nucleus are both basophil, the nucleus being rich in chromatin, and therefore staining deeply. In specimens stained by certain methods, however, the protoplasm shows a greater affinity for the dye than does the nucleus. In these cases the nucleus appears as a relatively light spot, surrounded by a more deeply stained protoplasm. With methylene blue and similar dyes the protoplasm shows uneven staining, which is due not to the presence of granules but to the possession

of a reticulum. The periphery of the cell is not always quite smooth, at any rate in the larger forms, but somewhat ragged and frayed. In a small proportion of these cells the nucleus is not quite round, but may be kidney-shaped, or sharply indented on its inner surface. The protoplasm possesses only a feeble affinity for acid or neutral dyes, and as a consequence in films stained by the triacid mixture, or with hæmatoxylin and eosin, the small lymphocyte appears only as a faintly or deeply stained apparently free nucleus. In the larger forms also the protoplasm, by these methods, is only faintly stained. By using the Romanowsky's stain, violet-red coloured granules may be demonstrated in a certain proportion of these cells. They vary greatly in size and number, are not found in other methods of staining, and may not be true cell-granules in Ehrlich's sense. These cells are the young cells of Uskow and his school, and the small hyaline cell of Sherrington, and Kanthack and Hardy. About 2000 of these cells are found per c.mm.

(2) *The Large Mononuclear Leucocyte* is sharply distinguished by Ehrlich from the lymphocytes. He describes them as large cells, two or three times as large as a red cell. They "possess a large oval nucleus, usually eccentrically situated, which stains faintly, and is surrounded by a relatively large amount of protoplasm. The latter is free from granules, feebly basophil, and, in contrast to the lymphocytes, stains less deeply than the nucleus." These cells change in the blood into the next kind. They form the largest type of leucocyte found normally in the circulation, and may reach the size of 15 μ. This is the large hyaline cell of Kanthack and Hardy.

(3) *The Transitional Form* is distinguished from the foregoing by a considerable indentation of the nucleus, by a somewhat greater affinity of the nucleus for basic dyes, as well as by the appearance in the protoplasm of scanty neutrophil granules. Groups 2 and 3 together form from 2 to 4 per cent of the total leucocytes, that is to say, about 200 to 300 are present in a c.mm. of blood.

(4) *The Polymorphonuclear Leucocyte.*—Originally called the polynuclear leucocyte, it has in addition been described by the terms neutrophil and finely granular eosinophil, and corresponds to the ripe cell of Uskow. These cells constitute about 66 per cent of the total number of leucocytes, and there are therefore normally about 5000 of them in a c.mm. of blood. They arise in small part, according to Ehrlich, from the transitional forms in the blood. They are rather smaller, about 12 μ or 13 μ, than either the large mononuclears or transitionals. The nucleus is peculiarly polymorphous, rather slender, and stains deeply, owing to richness and condensation of its chromatin. The nucleus often gives the impression of being divided into two or three parts, but in properly prepared specimens connecting strands can always be demonstrated between the lobes of what is in reality a single nucleus. A true fragmentation of the nucleus can be seen occasionally in the blood during life, though not in health, and is common in exudations. The protoplasm of the cell is thickly set with fine granules, which are not all of exactly the same size,

but never vary to an extent which would render them liable to be confused with either eosinophil or basophil coarse granules. The granules undoubtedly stain best with Ehrlich's neutral dyes, and were therefore called by him neutrophil granules. Under certain conditions they stain with acid dyes almost in the true eosinophil tint, and Kanthack and Hardy, who drew special attention to this point, proposed to call them the finely granular eosinophil (or oxyphil) leucocyte. A very short experience, however, will convince any one that their affinity for acid dyes is but seldom comparable to that possessed by the coarse granules of the eosinophil cell proper. That the granules of both these cells vary in their staining reactions is now well recognised, and, indeed, Ehrlich long ago pointed out that the neutrophil granules of the common granular myelocyte have in the early stages a considerable affinity for basic dyes. This affinity disappears in their descendants under normal conditions before they enter the blood-stream, but in myelogenic leukæmia it can be easily demonstrated in a certain number of the cells. That neutrophilic granules sometimes show more than the usual affinity for acid dyes is but due to an exaggeration of the change which takes place normally during their development, and does not, any more than the early basophilic tendency, disprove a specific granulation.

In specimens stained with the triacid mixture the nucleus appears green or greyish blue. The granules are a deep violet-red, and in cells which have been well spread out the protoplasm is sometimes stained a faint red colour. In specimens stained consecutively with methylene blue and eosin the nucleus appears a deep blue, but the result, as regards the granules, is most inconstant; sometimes they fail to stain at all, most often the protoplasm shows a diffuse eosin coloration, and in the most successful cases the granules appear well defined and of a true eosin colour. With the compound eosin-methylene blue stains — Jenner's, Leishman's, or Wright's—again, the staining of the granules is uncertain, but in satisfactory specimens they are pink. With Jenner's the nucleus is stained blue; with Leishman's or with Wright's purple.

(5) *The Eosinophil Cells* are about the same size as the polymorphonuclears, if anything rather smaller, and form about 1 to 3 per cent of the total, the average number being about 150 per c.mm. of blood. They contain coarse rounded granules, which stain deeply with acid dyes. Stained with eosin and methylene blue, they take on a pure eosin colour; in well-fixed triacid specimens they are orange-red. The nucleus is, as a rule, neither so polymorphous nor so slender as in the neutrophil cells, and is often horse-shoe shaped or bilobed. It stains less deeply, as a rule, than does the nucleus of the polymorphonuclears, whatever the method employed.

(6) *Coarsely granular basophilic or Mast-Cells* are, as a rule, obviously smaller than the polymorphonuclears or the eosinophils, and measure about 10 μ in diameter. In health they are never present in the blood in a percentage higher than ·5, and their total number in a c.mm. of blood is always under forty. Their prominent character-

istic is the possession of granules which stain only with basic dyes. The individual granules vary considerably in size even in a single cell, sometimes being much larger even than the coarse eosinophil granules, sometimes smaller, but on the whole they are considerably larger than the neutrophil. Another peculiarity is that with the majority of basic dyes they stain metachromatically, and not in the pure colour of the dye. With thionin, toluydene blue, and most samples of methylene blue they stain some shade of purple. They are exceedingly sensitive to water, and are especially well preserved if fixed by immersion of the wet film in boiling alcohol. In triacid specimens the granules do not take up the methyl green, but sometimes unstained areas or dots surrounding the nucleus indicate their position. With this mixture the form of the nucleus can best be seen, for it stains but faintly as a rule, and is greatly obscured by the partly overlying granules when these take up a dye. It is polymorphous, often trilobed in shape, and the fact that the chromatin is not condensed explains the feebleness of its staining capacity.

Abnormal Leucocytes found in the Blood.—The numbers of the leucocytes already described, which are present normally in the blood, may vary within narrow limits in health, while in disease the limits are widely increased. Further, cells smaller or larger than natural, cells showing a sparcity of granules, or divergences from the normal staining reactions, or other minor differences, are found in many departures from health. In addition, however, there appear in diseases, sometimes in enormous numbers, leucocytes which are never, in health, seen in the peripheral circulation.

Myelocytes may be divided, according to the granules they exhibit, into three classes, viz. Neutrophil, Eosinophil, Basophil.

The name myelocyte, when used without qualification, refers, as a rule, to the neutrophil myelocyte.

The Neutrophil Myelocyte.—These cells are for most part large—many of them being 15 μ or more in diameter. In myelogenic leukæmia, where they are seen in enormous numbers, the variations in size are very striking, giants of 20 μ, dwarfs of 10 μ, and myelocytes of every intervening grade being present. In conditions such as diphtheria, for example, where their presence is occasional and transient, and where their numbers do not reach a high standard, this striking variation is not seen. The nucleus is simple, rounded, or oval, and may occupy the centre of the cells when the protoplasm is scanty, or may be eccentrically placed when the protoplasm is relatively large in amount. The protoplasm contains fine neutrophil granules resembling those of the polymorphonuclear neutrophils. In triacid staining the nucleus is most often a pale green, more rarely a greyish blue. The granules are, typically, stained a violet-red, but often take on a dark brown or coppery tinge. With methylene blue and eosin used consecutively the nucleus stains pale blue. The granules when successfully stained appear as fine red or pinkish dots set in a background of strongly basophil protoplasm. In less successful specimens, in which the

specimen has not held the eosin well, these cells, because of this basophil property of the protoplasm, may be confounded with cells of the lymphocyte series if care be not taken. With compound eosin-methylene blue stains the granules stain pink, or, if they have not lost their youthful basic affinity, reddish blue.

Eosinophil Myelocytes.—These bear the same relation to the eosinophils of the blood that the neutrophil myelocytes do to the polymorphonuclears. In myelogenic leukæmia they may be seen in large numbers; they vary greatly in size, and, like the neutrophil myelocytes, show a tendency to depart from their normal staining reactions, and also from the regularity in size of their contained granules. The nucleus is rounded or oval, and stains faintly with all dyes. With triacid staining the granules of many of the cells are stained a dark brown or coppery red. With methylene blue and eosin they show some tendency to take up the basic stain.

Mast-Cell Myelocytes.—These cells, along with increased numbers of the normal mast-cells, are found in the blood in myelogenic leukæmia, and practically in no other condition. They show in this condition wide variations in the size of their granules, the usual differences being exaggerated. The cells themselves, too, are sometimes considerably larger, sometimes smaller than natural. The nucleus is oval or rounded, and the granules, though less liable to depart from the staining reactions of the normal type than the neutrophil or eosinophil myelocyte, do not always show the striking metachromatism usually seen in normal blood.

Both in lymphatic and myelogenic leukæmia cells may be seen in the blood resembling those of the lymphocyte series, but varying from them in certain respects, such as size or depth of staining; but whether these are abnormal cells of one of the normal types of this series, or whether they may not, or at any rate some of them, represent cells farther back in the genealogical tree of leucocyte development, remains an open question, and, so far as we know, is of no practical clinical moment.

Leucocytosis.—Leucocytosis is the term applied to an abnormal increase of the number of the leucocytes in the peripheral blood. It is often a transient condition, but may be prolonged, and may persist, as in malignant disease, up to the time of the patient's death. In the first place, it is important to understand what may be regarded as the normal leucocyte-count as well as to remember the physiological factors which may cause variation from the habitual standard of the individual. Sufficient attention has perhaps not been paid to what may be called the individual standard. When care is taken to exclude all disturbing factors, the number of leucocytes in any given individual in health varies within very narrow limits, but we have sufficient evidence to show that in different individuals the numbers may diverge widely. This point is of real importance, for what is a normal count for one person would for another mean a pathological increase. The obvious moral to be drawn from this circumstance is that every opportunity should be taken when occasion offers, as when a patient enters a hospital, to determine by

routine examination the standard for each individual, so that, should the examination of the blood become of importance, we may start with a better foundation to our knowledge. If, fortunately, this personal standard is known, and all possible sources of error are borne in mind, any increase which is greater than can be ascribed to instrumental error, in other words, to errors of observation, is a leucocytosis. In practice this knowledge is usually wanting, and some arbitrary standard is required; thus any count above 10,000, especially if the increase appears to affect one variety of cell only, is probably abnormal. In the healthy adult the mean number of leucocytes may be taken as 7500 per c.mm. of blood. Of these about 5000 will be polymorphonuclears, about 2000 lymphocytes and large mononuclears, and about 150 eosinophils. Mast-cells may reach a maximum limit of 40. The large mononuclears may, for clinical purposes, be grouped with the large and small lymphocytes, as their diagnostic value is at present doubtful, and a division of the two classes often a matter of some difficulty. Increases or decreases in the total number per c.mm. are in the majority of cases due to the increase or decrease of one variety of leucocyte; at any rate an increase of all varieties in proper proportion is always physiological. If in a count, whether high or low, different types are present in the usual proportion, it is more than probable that the total, whatever it may be, is normal for that individual.

Leucocytosis may be either *physiological* or *pathological*. Physiological leucocytosis occurs in infancy, during digestion, in pregnancy, and as the result of exercise and of hot and cold baths. These fluctuations, which might be ascribed to some pathological condition, must always be borne in mind in diagnosis.

Leucocytosis of Infancy and Early Childhood.—It has been shown by Rieder, Gundobin, Carstanjen, and Hutchison that immediately after birth the total leucocyte-count is about 18 to 20,000 per c.mm., and of these cells as many as 15,000 are polymorphonuclears, leaving a diminished proportion, but still absolutely higher number of lymphocytes, as compared with the adult. By the end of the first week this polymorphonuclear excess has disappeared, and the absolute number of this form has reached the figure at which it remains during life. At the same time a further increase in the number of lymphocytes takes place, and reaches its maximum about the age of six months. The number of lymphocytes then gradually falls, is still well marked at the end of the second year (twice the normal), and disappears usually about the seventh year. The number of lymphocytes at the end of the sixth month may be as high as 8000 or 9000, that is to say, four times the number found normally in adult life. This lymphocytosis, which is often increased in disease, is universally recognised as a common condition in early childhood. What is not understood so clearly as it should be, is that quite early the polymorphonuclears have settled down at the adult standard. We know that those conditions which are accompanied by an increase of the polymorphonuclear cells in the adult have exactly the same effect in children of

all ages. These facts, to my mind, support very strongly the opinion that the needs of the child in respect to this cell, and its polymorphonuclear reactions, are identical with those obtaining in older persons. The lymphocytic excess in early childhood, therefore, is not caused by any necessity for the vicarious performance of the functions of polymorphonuclear cells, but must be due to a special need of the body at this age in health. The same is probably true also of the further increase in disease, and it is unnecessary to ascribe the condition, as is not infrequently done, to a reversion to a fœtal type. This point is, I believe, of the highest importance to the proper conception of leucocytosis in children. It is hardly necessary to point out that at this age there is a much greater activity and a greater liability to disease of the lymphatic tissues throughout the body.

Digestion-Leucocytosis.—This is the form of physiological leucocytosis which most often obtrudes itself in our estimations. It was first shown in man by von Limbeck that the ingestion of food is followed, as a rule, by an increase per c.mm. in the number of leucocytes, and subsequently Rieder confirmed these observations, and proved further that animal proteid substances produced a greater effect than any other food. Sometimes this digestion-leucocytosis fails in the apparently healthy; and it is now recognised that very trifling factors, such as anæmia, delayed digestion, and constipation, may cause the phenomenon to remain in abeyance. Notwithstanding these exceptions, it is found, as a rule, that a meal rich in animal proteid causes an increase of about 30 per cent in the total leucocyte-count. In actual number this is so small (under 2500 per c.mm.) that the number present before the meal must be ascertained, if the result is to be of any value. Von Limbeck, for example, found in a well-nourished man 12,000 before and 14,000 after a meal, while in a beggar woman with no organic disease the numbers were 3000 before and 5400 after. The height of the leucocyte-curve is reached about three or four hours after a meal. This affords the necessary indication for eliminating it as a disturbing factor. In practice the most favourable time for obtaining the blood for examination is shortly before the principal meal of the day, or not till five or six hours after. It has been suggested that a count made early in the morning on a fasting patient would be more completely free from any digestive increase, but at this time the subject has usually fasted for a considerable number of hours, and the count is then unduly low, showing in a minor degree the leucopenia of starvation. Opinions differ as to the type of leucocyte which forms the increase in numbers. Rieder says the lymphocytes, Japha the polymorphonuclears. I believe that both are increased, but that if numbers are given and not percentages it will be seen that the lymphocytes show a greater proportional rise. Müller was the first to point out that in carcinoma of the stomach digestion-leucocytosis did not take place; but exceptions to this rule, and the occasional absence of this phenomenon in other conditions, have deprived this observation of most, if not of all, its diagnostic value.

In children the increase is as a rule larger, but the great increase occurring in the newly born, which has sometimes been ascribed to the commencement of feeding, is clearly not due to this alone.

Leucocytosis in Pregnancy.—It has been generally held, on the authority of Halla, von Limbeck, and Rieder, that a slight leucocytosis occurs towards the end of pregnancy, and is more marked and more constantly present in primiparæ, but recently Hahl and Zangemeister have denied its presence in this state. So many disturbing factors arise during the puerperium that no reliance can be placed on any "physiological" leucocytosis at this time.

The transient variations taking place as the result of *hot or cold baths* are probably only local variations in the skin due to the action of heat or cold on the peripheral vessels. Provided the possibility of these variations is known, they are easily eliminated as a disturbing factor. The same is true of the increase that follows severe exercise; the cause of this leucocytosis is unknown.

Pathological Leucocytosis.—This class is commonly subdivided into: (1) Inflammatory leucocytosis, (2) Toxic leucocytosis, (3) Leucocytosis accompanying certain anæmic conditions, especially post-hæmorrhagic anæmia, and (4) Leucocytosis in various cachexias. Under the head of Inflammatory is classed the leucocytosis found in certain specific infections, *e.g.* diphtheria, and it would be simpler and less open to objection if the term inflammatory were abandoned and the term infective substituted.

The term leucocytosis, when used without qualification, most commonly means a polymorphonuclear leucocytosis, for this is by far the commonest form of increase; yet it is important to remember that, theoretically at any rate, the increase may be due to any form singly, the number of the other forms remaining unchanged, or to any combination of the different forms usually present, or even to the presence of abnormal cells. Moreover, it happens not infrequently that at the time one variety is increasing another may be diminishing. It is clear, therefore, that in many cases a differential leucocyte-count is absolutely essential if full use is to be made of the information obtainable; but when the character of the leucocytosis is not in doubt a mere count of the total number will give all the information required.

The term *lymphocytosis* is used to indicate an increase affecting the total of lymphocytes. The term *relative* lymphocytosis, sometimes applied to conditions where the number of lymphocytes may be normal and the number of polymorphonuclears diminished, is so misleading that it should be rigorously excluded. Where both forms are increased, the proportion of increase of the lymphocytes may be larger than that of the neutrophils, but even that condition is imperfectly described by this term. All such difficulties would, of course, be obviated if, in recording differential counts, the custom became universal of stating absolute numbers, per c.mm., as well as percentages. The terms eosinophilia and basophilia should in the same way be employed only when the actual number of these cells is increased.

Inflammatory Leucocytosis or the Leucocytosis of certain Infective Diseases.—Pneumonia, scarlet fever, plague, whooping-cough, small-pox in the eruptive stage, chicken-pox, secondary syphilis, acute rheumatism, cholera, relapsing and typhus fever, are all of them accompanied by some degree of leucocytosis. In infections with pyogenetic organisms, whether the condition lead to a gumboil or a carbuncle, a small patch of cutaneous erysipelas or an acute streptococcal septicæmia, or any of the multitude of other lesions due to this cause, an increase of the leucocytes often occurs. The degree varies, and though it cannot, as v. Limbeck suggested, be shown to bear any strict relation to the amount of "exudation" or to run exactly parallel to the height of the temperature, yet with certain reservations some relation between these various signs may often be observed in the course of an infection. The total number of leucocytes in about 40 per cent of the cases lies between 15,000 and 20,000 per c.mm., while of the remainder a greater proportion will be below rather than above these limits. Counts above 30,000 are not common, and above 50,000, in my experience, rare. The polymorphonuclears alone are increased as a rule, while the eosinophils are diminished sometimes very markedly, as in pneumonia; the lymphocytes remain unaltered, though occasionally these also show an absolute decrease. The course taken by the leucocyte-curve naturally depends on the nature of the affection. In certain diseases of well-defined duration, *e.g.* pneumonia, the leucocytosis is present in the initial rigor, remains at a high level during the course of the fever, and begins to fall rapidly at or shortly before the crisis. A failure in the appearance of this rapid fall occurs in cases in which resolution is delayed, or some complication, such as influenza, exists. When the leucocyte-curve approaches the normal the eosinophils increase again in number, and may even for a time exceed the average. In conditions with a less regular course the correspondence between the temperature- and leucocyte-charts is less exact, but on the whole they show a certain parallelism. Fever of itself is not a sufficient cause of leucocytosis, as may be seen in typhoid fever, so that the cause of this synchronous fluctuation must be ascribed to some more fundamental cause common to both.

The Significance to be attached to Inflammatory Leucocytosis.—We probably know more of the leucocytosis attending appendicitis than of that in other similar conditions, but the details about to be given of this affection may be applied to the rest. When the leucocyte-count is low, several explanations are possible. The infection may be a very mild one resulting in a hardly noticeable alteration, or the infection may be very severe, so that the body is powerless to react; or again, in cases of some duration, the inflammatory process may have become shut off, absorption may have ceased, and the mechanism of leucocytosis have failed from the absence of stimulus. This is a striking example of the necessity in every case of weighing well the history and clinical symptoms, for with their aid there should be little doubt which of the three alternatives is present. It will be noticed, too, that pus may be present without any leucocytosis.

When the leucocytosis is moderate in degree—under 20,000 but over 15,000—the infection is of appreciable severity, but it is not possible to say whether pus is being formed or not. The reaction of the body is well marked, and for the time being at any rate, whatever his condition, the patient is making some kind of fight. In larger counts above 20,000 the infection is always severe; there may be a large abscess, a gangrenous appendicitis, or general peritonitis, the high count at the same time pointing to a favourable reaction. A discovery of these facts would point to the necessity for operation if the count is above 20,000; and some would fix a lower number, 18,000, as the figure which should negative any delay.

Thus far only single counts have been taken into consideration. Their value has been shown, but the information to be derived from repeated counts is much greater. By this means the course of the disease can be gauged with something approaching accuracy. In mild infections a progressively increasing count may be the only sign of the extension of the disease, and on the other hand a decreasing count is good evidence that the inflammation is subsiding. If a count, at first moderate, should be found gradually increasing, the disease is probably extending; and if the level of 18,000 or 20,000 be reached, there is a strong probability that suppuration is taking place. On the other hand, a decrease in such circumstances would justify delay in operating unless the clinical symptoms are increasing in severity. In counts of over 20,000 which remain stationary, where we may assume on clinical grounds that the morbid process is not extending, the probability of abscess-formation is very great. In high or even moderate counts there is the possibility that a *decrease* may point to a deficient reaction, and be of very serious prognostic import. After an appendicular abscess has been opened, the count rapidly falls as absorption ceases; and a failure in this diminution, or a subsequent increase of the count, points very strongly to imperfect drainage or to extension of the process.

Results comparable with these are found in other infections with pyogenetic organisms, if allowance be made for obvious differences due to the characters of the different conditions. In cases of chronic malignant endocarditis, in which the symptoms referable to the heart predominate, there is often a complete absence of leucocytosis, and this at a time when streptococci may be found circulating in the blood; the infecting organism is of low virulence, and the local condition is of much the greater importance. In cases of greater severity, which sometimes simulate typhoid fever, there is a marked leucocytosis; and again in exceedingly severe cases, those which are practically acute septicæmias with cardiac lesions, the leucocytosis may be entirely absent. The prognosis for all cases of malignant endocarditis is, of course, practically hopeless, and the degree of reaction found takes us no farther. The presence of a leucocytosis in doubtful cases may, however, be of the greatest assistance; for example, in excluding typhoid fever or miliary tuberculosis.

In pneumonia, as in appendicitis, a mild infection with a sufficient reaction causes a slight leucocytosis. A more severe infection with a good reaction gives rise to a marked leucocytosis, while in severe infections with feeble reaction leucocytosis is absent. The prognosis is always favourable in the first category, always unfavourable in the third, and in the second doubtful. Space forbids further details about the numerous conditions falling under this heading, but these examples show what may be expected and learnt as regards this group.

The mere presence or absence of a leucocytosis may be a sign of the greatest value. Of the infective fevers some are accompanied by leucocytosis, some are not. A list of those in which it is usually present has been given above; those in which it is absent comprise typhoid fever, influenza, measles, German measles, malaria, Malta fever, and mumps. In pure infections with the tubercle bacillus, leucocytosis is, as a rule, absent; but in tuberculous meningitis, and to a certain extent in tuberculous affections of serous membranes, the exceptions to the rule are sufficiently numerous to detract greatly from the value of this means of distinguishing between the tuberculous and other forms. Why the blood in some infective diseases shows a leucocytosis which is absent in others is unknown. That the mechanism of its production is not destroyed is shown by the fact that when, for example, in typhoid fever, some complication occurs, such as perforation of the intestine or pneumonia, a leucocytosis appears, just as it would in those conditions when uncomplicated. The course of the leucocytosis in the infective fevers and its significance are much the same as in pyogenetic infections; certain minor differences, however, show themselves in individual cases.

The increase again is commonly limited to the polymorphonuclears, and the eosinophils are usually diminished. In whooping-cough and in small-pox, however, the lymphocytes are notably increased, as they are in secondary syphilis. In scarlet fever the eosinophils are increased, especially, according to Neusser, in cases running a favourable course.

In diphtheria Ewing observed a reduction in the degree of leucocytosis after the administration of antitoxin in all cases except two, which were fatal. Perhaps the greatest value of leucocytosis is in enabling us to distinguish between two diseases, *e.g.* scarlet fever and measles, one of which is accompanied by leucocytosis, while the other is not.

Toxic Leucocytosis.—In this class the leucocytosis is usually of the polymorphonuclear type. The ingestion or hypodermic injection of certain drugs, even in medicinal doses, may give rise to an increase in the number of leucocytes. Potassium chlorate, the salicylates, antipyrin, antifebrin, phenacetin, digitalis, the oils of cinnamon and peppermint, and camphor, among other substances, cause a leucocytosis which usually appears early, is moderate in amount, and disappears in two or three hours. The knowledge of these facts, so that allowance may be made for them, is important, but otherwise is of no clinical value. The injection of tuberculin, thyroid extract, or pilocarpin is followed by an increase in the number of lymphocytes.

In uræmia, cirrhosis of the liver (especially in Hanot's form), and in food poisoning the leucocyte-count may be raised.

Leucocytosis in Malignant Disease and certain Cachexias.—In many chronic wasting diseases leucocytosis may be present. It is due probably in the majority of cases to some toxic influence, but in others is caused by the secondary infections common in such conditions.

In malignant disease, when the primary growth has reached any material size, an increase, usually moderate in degree, is almost always found; and, if persistent, such increase may sometimes be of use in distinguishing between malignant disease and other conditions, such as aneurysm, which are not accompanied by leucocytosis. The absence of a leucocytosis, however, will not suffice to exclude malignant disease—in cancer of the stomach even when advanced leucocytosis is often absent. At present we do not possess sufficient evidence to justify any statement as to the influence on the blood-count of the situation of the growth. Bone-marrow, glands, and skin may be affected without, except in isolated cases, showing any variations from the usual type in the variety of leucocytes present. On the whole, sarcoma is prone to give rise to more marked changes than carcinoma, and in a few cases a great increase in lymphocytes has been noted, but in all forms the increase is usually polymorphonuclear. I have seen a polynuclear leucocytosis of 60,000 in a rapidly-growing sarcoma of the kidney in a child of six. A very full account of this subject with references is given in Cabot's book.

The Leucocytosis accompanying certain Anæmias, especially Post-hæmorrhagic Anæmia.—In pernicious anæmia the number of leucocytes is usually diminished, though not infrequently the number is raised during periods of improvement. The decrease affects almost entirely the polymorphonuclears, so that a "relative" lymphocytosis is often described. In extreme cases the lymphocytes also may show some diminution. In the majority of cases of chlorosis the white count is normal, but an excess of lymphocytes has been noted in severe cases. After large hæmorrhages a leucocytosis appears almost immediately, which rapidly disappears again as the volume of the circulating blood is restored. This is due to the flow of lymph from the tissues into the blood-vessels. In secondary anæmias leucocytosis is often absent, and when it occurs is a result not of the anæmia but of the primary disease.

Leucocytosis appears frequently in moribund patients, and when it is not due to some terminal infection is the result of stasis in the peripheral vessels.

Lymphocytosis.—Absolute increase in the number of lymphocytes without increase in the number of the other varieties is rare. It is seen in young children in health. An increase beyond the normal number is also seen in young children in many conditions where the number of the other cells is altered. In congenital syphilis, in whooping-cough, in gastro-intestinal disorders, in rickets, and in the condition known as anæmia pseudoleukæmica infantum (von Jaksch's) the number of lymphocytes is absolutely and relatively high. That this depends

entirely on the age of the patient, as is often assumed, I do not believe. In one well-marked case of von Jaksch's disease the supervention of acute osteomyelitis caused a large increase, composed almost entirely of polymorphonuclears, in the already high leucocyte-count. As has already been mentioned, the injection of tuberculin or pilocarpin, or the administration of thyroid extract, is followed by a lymphocytosis. In the writer's experience the majority of cases of affections of the lymphatic glands, such as Hodgkin's disease and tuberculosis, run their whole course without any variation from the normal; and although high (and low) counts are not infrequently found, it would appear more probable that they are due to accidental causes and do not form an integral part of the disease itself. When an increase does occur, it usually affects the polymorphonuclears, though many scattered cases of increase of the lymphocytes in Hodgkin's disease are recorded. In secondary syphilis an increase of lymphocytes is often present along with glandular enlargement. In sarcoma of the lymphatic glands there is sometimes, though by no means constantly, an increase in the number of lymphocytes. On the other hand, Reinbach has reported a case where the lymphocytes formed only 0·6 per cent of the total leucocyte-count.

In those conditions in which the total number of leucocytes per c.mm. is diminished the decrease is nearly always due to a diminution in the polymorphonuclears. This is commonly called a relative lymphocytosis. Typhoid fever, malaria, influenza, Graves' disease, pernicious anæmia, and chlorosis often show a relative lymphocytosis. In lymphatic leukæmia the lymphocytes form an enormous proportion of all the leucocytes, over 95 per cent in many cases, the polymorphonuclears remaining about the normal standard, while the eosinophils are, if anything, diminished. In myelogenic leukæmia also the lymphocytes, though present in diminished proportion, are nearly always increased considerably in numbers.

Eosinophilia.—Eosinophil cells are present normally in increased numbers in the blood of infants and young children. In most infective diseases which are accompanied by a leucocytosis, excepting scarlet fever, and especially in pyogenetic infections, the number of eosinophils, which is diminished during the height of the disease, increases again, and may exceed the normal standard for a time during convalescence. Owing to the labours of Zappert, Neusser, and many others the number of conditions in which eosinophilia may be present is known to be very large. In many skin diseases, especially in pemphigus, dermatitis herpetiformis, urticaria pigmentosa, and lupus, but less constantly in other forms, an increase of eosinophils, amounting to several thousands, has been noted by many observers. On the other hand the numbers are sometimes found not to be raised. I believe that this discrepancy is due to the fact that, even in the conditions where eosinophilia has been found with the greatest constancy, it is only present during exacerbations of the disease. In one patient with pemphigus, in whom, the day after a fresh crop of vesicles appeared, the eosinophils were 16,000 per

c.mm., the count reached the normal within a week in the absence of any further eruption of bullæ. The increase does not depend therefore on the presence or the extent of the skin lesion, but on some underlying cause which excites both the eosinophilia and the eruption. In the case of an enormous blister caused by a scald I failed to find any increase at all. They are increased in true spasmodic asthma, and, Neusser asserts, in all uric acid diseases. Our knowledge of the eosinophilia in the blood of persons harbouring worms has recently been considerably extended. Almost any form may cause an increase of these cells in the blood, though the highest counts have been found in trichinosis, ankylostomiasis, and bilharzial infection. Indeed, the occurrence of eosinophilia without obvious cause may now well arouse a suspicion of the presence of some parasite. Dr. Boycott has shown that an examination of the blood is the easiest and quickest way to determine whether in large bodies of men the probability of infection is great enough to warrant a systematic search for the eggs of ankylostoma in the stools. In 94 per cent of the cases of ankylostomiasis which he examined he found more than 8 per cent of eosinophils and an average of 18 per cent. In his paper he gives a full account of the other conditions in which eosinophilia is found, and is careful to point out the limitations of its value in diagnosis. In myelogenic leukæmia the number of eosinophils is always increased, sometimes very greatly, though their proportion may be normal. In this condition many of the cells bearing eosinophil granules are myelocytes. In anæmia pseudoleukæmica infantum both varieties of the eosinophils are present as a rule, the ordinary form in increased numbers.

Neusser's paper contains a long list of conditions in which eosinophilia may exist, with a highly coloured picture of its diagnostic uses.

Basophilia.—But little is known of this condition. The only disease in which it constantly appears in a marked degree is myelogenic leukæmia; the writer has seen as many as 16,000 and 28,000 in two cases, forming 23 and 18 per cent of the whole number of leucocytes. A. Taylor has noted an increase in a case of carcinoma without bone metastasis, once each in gonorrhœa and mycosis fungoides, and twice in "septic" bone disease. It is occasionally present in von Jaksch's disease, and Dr. Boycott draws attention to counts above the accepted standard in cases of ankylostomiasis and also in health.

Myelocytes (Neutrophil).—Attention has been drawn to the presence of eosinophil myelocytes in myelogenic leukæmia and von Jaksch's disease; and in these conditions neutrophil myelocytes also appear in large numbers in the blood; in the former the number may be enormous, 100,000 or more. Though in other conditions (neutrophil) myelocytes are occasionally found, the numbers are never very high. Rieder, Engel, and Türk have established their appearance in infective diseases, and they are found not unnaturally sometimes in diseases showing an ordinary neutrophil leucocytosis, such as pyogenetic infections, cachexias, and toxic conditions. They are also often seen in pernicious anæmia.

Animal Parasites

The Malarial Parasite.—The simplest method of demonstrating the presence of the malarial parasite in the peripheral blood is by the examination of a fresh film. For this purpose scrupulously clean slides and cover-glasses are required, and the film must be thin. The specimen is examined at once with an oil-immersion lens. When the parasites are fairly numerous and have already developed their characteristic pigment, and the specimen is so prepared that the red cells lie separate and flat, there is no difficulty, after a little practice, in finding them by this method. It possesses the additional advantage that many biological characters can be observed, such as the streaming movement of the pigment granules, the intra-corpuscular amœboid movements of the parasite, and its gradual maturation. When the parasites are few in number and young the difficulty may be very great, even to an experienced observer. Dry and stained films in these circumstances render the demonstration much more easy. Specimens are best stained by Leishman's or Romanowsky's method. They may be stained with eosin and methylene blue after fixing in alcohol or methyl-alcohol; but this method, while sufficing for their demonstration, is inadequate if the fine and histological details of the parasite are to be studied. For the inexperienced the best time to take the blood for examination is about six or eight hours before an expected paroxysm; at this time the parasites are nearly full grown and are more numerous in the peripheral blood than during the ague-fit itself.

Trypanosomes in the blood, and the Leishman-Donovan bodies removed by puncture of the spleen, should also be stained by Romanowsky's method or Leishman's modification of it.

Filariasis.—The embryos of the different species, Filaria diurna, F. nocturna, and F. perstans, may be demonstrated in either fresh or stained films taken at an appropriate time. Because of the large size of the parasite the films need not be thin, and are indeed preferably thick. Dry films may be stained with eosin and methylene blue.

The Parasite of Relapsing Fever.—The spirochæte of relapsing fever is present in the blood during the continuance of the fever and during relapses, but with rare exceptions is absent during the afebrile periods. It is most easily demonstrated in stained films. In fresh films it is less readily found, but its motility can be demonstrated.

Hæmoglobinæmia.—This term is used to denote the presence of free hæmoglobin in the plasma. In extreme cases it is associated with hæmoglobinuria, as in paroxysmal hæmoglobinuria. The condition occurs in many circumstances—in severe infections such as variola or scarlet fever, in certain toxic states such as malignant jaundice, in snake-bite, poisoning by guaiacol, arseniuretted hydrogen, and after severe burns. Free hæmoglobin may be detected by the spectroscope in the plasma after centrifugalising the blood.

Methæmoglobinæmia.—More important than hæmoglobinæmia are the conditions in which the hæmoglobin is converted into methæmoglobin, usually after the destruction of the red corpuscles has liberated it. Chlorate of potash, antipyrin, acetanilid (antifebrin), phenacetin, have all been observed as the cause of methæmoglobinæmia. The condition may also arise in nitro-benzol poisoning. The blood is often chocolate-coloured, and the characteristic absorption-bands of methæmoglobin are present.

Carboxyhæmoglobinæmia.—The carbonic oxide compound with hæmoglobin is seen in cases of coal-gas poisoning. To the naked eye the blood assumes a cherry-red colour. As the spectrum absorption-bands resemble those of oxyhæmoglobin, the spectroscopic test, especially as oxyhæmoglobin is also present, is insufficient for diagnostic purposes.

The spectroscope best adapted for clinical examination is the small pocket spectroscope of Browning, which is furnished with a sliding tube

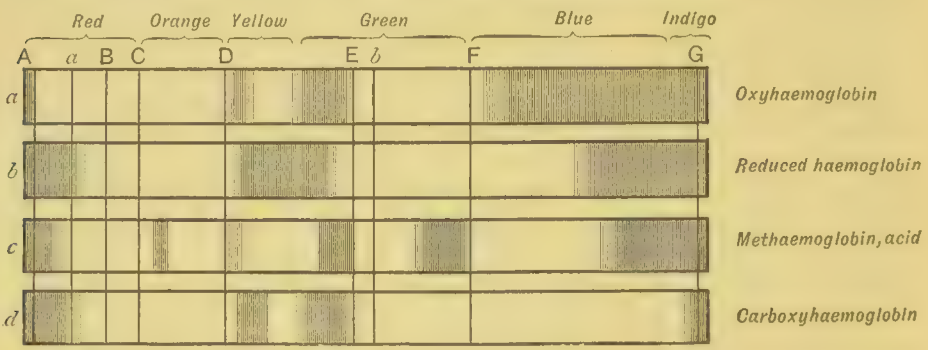


FIG. 61.

for focussing, and a slit-like aperture which may be used to regulate the amount of light admitted. The material to be examined is conveniently placed in flattened phials with parallel sides.

Estimation of the Total Volume of the Blood.—Our knowledge of the total mass of the blood and its variations in disease is very scanty. Till recently, indeed, we have had no method even approximately accurate by which it could be estimated. In the *Journal of Physiology*, vol. xxv., Drs. Haldane and Lorrain Smith describe a method which, were it not for the doubt raised by some of the remarkable results obtained by its use, would seem exact.

The patient is made to respire a mixture of air and oxygen contained in a small bag. The apparatus is so arranged that the carbonic acid, which would otherwise accumulate, is absorbed by soda lime, and oxygen is supplied as required. Into the bag measured quantities of carbon monoxide are introduced, and are gradually absorbed as the patient breathes the contents of the bag again and again. After allowing time for the complete absorption of the gas, a sample of blood is taken, and the percentage of carboxyhæmoglobin present is estimated. In this way the percentage of carboxyhæmoglobin in the whole blood after the absorption

of a known quantity of carbon monoxide is obtained. From this is calculated the amount necessary to convert the whole of the hæmoglobin into carboxyhæmoglobin, and, since the oxygen capacity and carbon monoxide capacity of hæmogoblin are the same, this gives the oxygen capacity for the whole blood. The oxygen capacity of the whole blood having been found, it remains to find the volume of the blood. By estimating the hæmoglobin in a measured quantity of blood by comparison with bovine blood, the oxygen capacity of which has been determined, the oxygen capacity of the given quantity may be calculated, and from this, the total capacity being already known, the total volume of the blood can easily be determined. The value of an accurate knowledge of the total mass of blood would be so great in many cases that it is to be hoped that the method will be tested by an extensive number of observations. Till the introduction of this method the only way of gauging the variations in the total mass of blood was by counting the corpuscles in a given volume at intervals. The experiments of Wörm-Müller and Cohnheim have shown that it is impossible to produce more than a very transient alteration in the volume of the blood. In transfusion experiments, for example, the vessels at first dilated to admit the excess, but in a short time, as shown by an increase in the number of red cells, a large part of the fluid left the vessels. These experiments pointed to the existence of a mechanism for maintaining the equilibrium of the mass of blood, and the possibility of such a condition as plethora seemed to be negatived. In man temporary variations are seen under many conditions, sweating or vomiting, or ingestion of large quantities of fluid, causing a rise or fall of the red count. In man, therefore, there exists also a mechanism by which variations in the total mass are corrected. It is, of course, possible to argue that in certain conditions this mechanism is disturbed, and it cannot be denied that such may be the case. It would appear from Prof. Lorrain Smith's observations that, in certain conditions, the regulating mechanism being disturbed, the mass of blood may be doubled, or more than doubled. It is still possible, in chlorotic women for instance, to produce transient variations, as in the healthy person. It must follow that the regulating mechanism is still capable of working naturally, but that the standard volume has been raised for the individual. This is, of course, possible. So many of our deductions are based on the constancy of the blood-mass that, if Prof. Lorrain Smith's results should stand the test of time, a very large number of usually accepted statements will possibly be found to have no foundation in fact. The following are some of the conclusions drawn by Prof. Lorrain Smith as the outcome of the application of this method in a large number of cases:—(1) The anæmia of chlorosis is due to an increase in the plasma of the blood, the total hæmoglobin remaining normal in amount; (2) in pernicious anæmia the total amount of hæmoglobin becomes reduced in proportion to the severity of the disease. The volume of plasma may be either increased or reduced. In anæmia after hæmorrhage the volume of the plasma is not much increased. Drs.

Boycott and Haldane have shown by this method that the anæmia of ankylostomiasis is of the chlorotic type—that is to say, the total hæmoglobin is normal, but the volume of the plasma is greatly increased.

Agglutination Reaction

To the discovery of *Pfeiffer's phenomenon*, followed by the researches of Bordet, and Gruber and Durham, we owe the employment of the agglutination reaction in the clinical diagnosis of typhoid fever. Widal and Grünbaum were the first to employ the test for this purpose, and Widal was the first to publish the results.

The substance which gives rise to the phenomenon of agglutination is, as regards certain organisms at any rate, present in the blood of a small proportion of healthy persons, though not, as a rule, in any high degree. It most commonly occurs under natural conditions in the blood of persons who are suffering from or have recently recovered from an infection with some specific organism, and is accompanied almost always by other substances, "anti-bodies," to which it is no doubt in some way related, though the degree to which the different bodies are present in the blood may not run a parallel course.

Technique.—The simplest way of performing the test, when it can be completed immediately, is to collect the blood and dilute it at once to the required standard. The site of the puncture should be cleaned, but need not be sterilised. With the leucocyte counter of a hæmocytometer the dilution presents no difficulties; the blood is drawn up to the mark 1, and then the diluting fluid up to the mark 11. The mixture in the bulb is then in a dilution of 1 in 10. Instead of the hæmocytometer an ordinary glass pipette (A or B, Fig. 62), with not too narrow a bore, may be used. A drop of blood having been obtained, one end of the pipette is applied to it, and the blood allowed to run into the capillary portion, care being taken to avoid the entrance of air-bubbles, which would break the column. A mark (*a*) is made with ink or a wax pencil at the spot reached by the column of blood, which is then blown out into a clean vessel. The marked pipette may then be used to make the necessary dilution 1:10. The diluting fluid used may be distilled water, physiological salt solution, or broth. If the diluting fluid is allowed to run up to the mark, and then a small air-bubble is allowed to enter, and the process repeated as often as is necessary, the required amount of fluid is easily measured (Wright's method). Blood and not serum having been taken in the first place, the

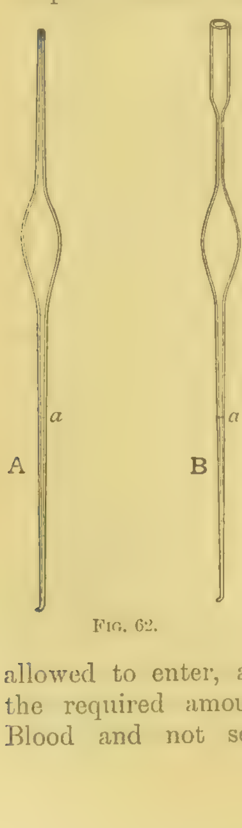


Fig. 62.

dilution will necessarily be higher than if the latter had been used. Allowing a proportion of 40 per cent of red cells in the total volume as a minimum for normal blood, a dilution of 1 : 10 will allow for a certain degree of anæmia, and yet equal a dilution of 1 : 15 of the serum alone. If the diluted blood is allowed to stand for a few moments most of the red corpuscles will sink, and the supernatant fluid will be sufficiently clear not to interfere in any way with the test. It is taken for granted that the strain of typhoid bacilli used has been thoroughly tested, and its reaction to agglutinating substances compared with that of standard cultures. In practice it is best to keep the stock cultures in the cold, and to make subcultures for use as may be required. The stock cultures will, of course, require to be transferred to fresh media from time to time, but this need not be done oftener than once a month. Where such tests are being carried out daily, perhaps the most convenient way is to make a subculture on gelatin every few days, and from this to prepare an emulsion in salt solution or broth as may be required. In our experience at St. Bartholomew's Hospital such a gelatin culture may be used with safety for four or five days, and even longer, and the resulting emulsions are in every way as suitable, and in some ways more free from certain sources of error than broth cultures, which must be made fresh every day and incubated at 37° C.

The emulsion is easily made by taking a small quantity of the solid culture on a sterile platinum loop, and moving it to and fro in a small quantity of broth or salt solution. In this way the bacilli are gradually dissolved off, and when a faint but obvious turbidity is reached the emulsion is ready for use. Equal parts of the diluted blood and of the emulsion (or broth culture) are measured on a cover-slip, either with a platinum loop or a marked capillary pipette. They are next thoroughly mixed and the mixture examined microscopically, either as a hanging drop or in the ordinary way as a wet film. The preparation should in either case be ringed round with vaseline or paraffin to prevent evaporation. The preparation, as finally obtained after mixing with equal parts of the emulsion or broth culture, will hold the blood in double the original dilution. On the same slide a control preparation of the emulsion itself should be mounted for comparison.

Observation should be commenced at once. In a few cases the bacilli may be found already clumped, partially or even completely, in the mixture. A glance at the control specimen of the emulsion will suffice to show whether this is due to some fault there, or whether the agglutination is due to the action of the diluted blood. In the great majority of the cases, however, the bacilli will be seen evenly distributed, quite separate, and very actively motile, darting rapidly in every direction about the field. When agglutination is about to occur the movements of the bacilli become sluggish. The bacilli then begin to adhere to one another, first in small groups of two or three; these groups gradually increase in size, till, finally, in what is called a complete reaction, all the bacilli are motionless and aggregated in large clumps, the intervening parts of the micro-

scopic field being clear. This appearance should be general throughout the preparation. In the control emulsion, or with an indifferent non-typhoid serum, the bacilli remain actively motile and quite separate for several hours at least. If the reaction be positive the test may be repeated with dilutions of 1 : 40, 1 : 60, or even higher, and the degree of certainty correspondingly increased.

Instead of blood either serum or plasma may be used; indeed, if great accuracy as to dilution is essential, as, for instance, in cases of comparative observations, one or other of those fluids must be used, and the dilutions carried out by means of accurately graduated pipettes such as those of the hæmocytometer. For clinical purposes the serum should be diluted 1:15 before being mixed with equal parts of the emulsion. The blood may be collected conveniently in a small U-tube, and the plasma obtained by centrifugalising, or it may be drawn into the bulb of a pipette (Fig. 62) and allowed to clot, and the serum used after it has been expressed. The serum or plasma, as the case may be, can then be used in the same manner as the blood after diluting.

Between the complete and the absolutely negative reaction every degree of agglutination can be observed, and not only are these differences in the degree of clumping observed, but differences in the rate at which it takes place also occur. The test had not been employed for clinical purposes for any length of time before it was revealed that the serum of certain healthy persons, and also of some persons with other diseases, possesses the property of agglutinating typhoid bacilli when a low dilution is employed; and it is clearly recognised now that before any conclusions may be drawn from the occurrence of agglutination two fundamental factors must be known: (*a*) the degree of dilution of the serum; (*b*) the length of time of observation. In other words, before any reaction can be accepted as complete, not only must the bacilli be completely agglutinated, but this result must have been arrived at within a certain standard time. The conditions of the test may be made more stringent by increasing the dilution or diminishing the length of time allowed, but, speaking generally, it is easier to exclude reactions in non-typhoid cases by raising the dilution than by curtailing the observation period.

In many cases a reaction will occur with non-typhoid serum in a dilution of 1:10, a few with 1:20; but above this standard the cases are rare. A dilution of 1:30 of the serum suffices to exclude the vast majority of such misleading reactions, and is preferable to any higher dilution which, while serving to exclude even the extreme among such, would at the same time fail to give a positive reaction in a large number of cases of undoubted typhoid. The observation-time should be limited to an hour. Dr. Horton-Smith's figures for the three years 1897-99, at St. Bartholomew's, showed that of 546 cases in which the test was employed, in only one of the 346 non-typhoidal was the reaction present, and in that case the patient had passed through an attack of typhoid fever four months before. At that

time the dilution in use there was 1:20, with a time-limit of two hours, which is proof that the more stringent standard now employed is indeed high enough for practical purposes.

The date at which the reaction appears is usually about the end of the first week, though it has been found as early as the fifth day, and a positive reaction has been recorded even on the third or second day. The indefinite onset of the disease is sufficient reason for regarding these very early cases with suspicion. After its first appearance it usually increases in degree and remains present throughout the disease, subsiding, as a rule, during convalescence. It may, however, disappear before the end of the attack, and occasionally is found on one or two occasions only, or may be absent throughout the whole course of the disease. The percentage of cases in which this last event occurs is very small, and generally it may be said that, if the limits of time and dilution given above are observed, the errors, either positive or negative, do not amount to more than 3 per cent of the whole.

In estimating the value of the test it is often forgotten that before its use became general the diagnosis of typhoid fever, in any given case, though finally clear, was often in doubt for many days, and that on the whole the presence of the reaction enables the diagnosis to be established at an earlier date; or, what is quite as important, the probability of the disease being other than typhoid is kept prominently in mind when, after repeated examination, the reaction is absent. In the majority of cases the reaction cannot be obtained after a year has elapsed, though it has been found after a much longer period (twenty-eight years in Widal's first paper).

The dried-blood method, introduced by Wyatt Johnston, is not much used in this country, but in America it is very largely employed, especially in public health work. A large drop of blood is collected on some clean non-absorbing surface, such as glass, and allowed to dry. In use the dried blood is dissolved in water, some attempt being made to gauge the dilution by means of the colour, and the rest of the test is carried out in the ordinary manner. The advantages of the method lie in the simplicity with which the blood can be obtained, and its portability, as well as in the fact that dried blood does not offer a good medium for the multiplication of saprophytes. On the other hand, the dilution is very much a matter of guess-work, though it should not be difficult to secure at least the dilution necessary for safety.

The test may be performed with the aid of cultures which have been killed by heating to 60° C. for ten minutes, or by adding a small quantity of formalin; these dead cultures are, however, not so sensitive to the agglutinating substance.

In the clinical application of the test, observation of the reaction is almost invariably carried on by means of the microscope, but the same phenomenon may be observed with the naked eye. If a sufficient proportion of active serum be mixed with a recent broth culture or suspension of active typhoid bacilli placed in a small tube, the uniform turbidity is

replaced after a time by a granular appearance, due to the clumping of the bacilli, and the clumps in time fall to the bottom of the tube and form a sediment, leaving the broth clear above. This is known as the sedimentation test.

The agglutination reaction is not confined to typhoid infection, and attempts more or less successful have been made to employ the test in the diagnosis of other conditions. The relation of the typhoid reaction to certain organisms of the typhoid group is discussed in the article on enteric fever.

Agglutination Reaction in Malta Fever.—Drs. Wright and Smith found that the serum of patients suffering from Mediterranean fever clumps the micrococcus melitensis, and since their observations the value of the test has not only been confirmed, but the geographical distribution of this disease has been proved to be much wider than was at one time thought. It may appear by the third day and persists for months. A dilution of 1 : 50 with a time-limit of half an hour is recommended. The organism is a slow-growing one, so that a "young culture" means four or five days, and it may be necessary to filter the emulsion before use in order to remove small clumps.

Agglutination Reaction in Plague.—Although agglutination has been demonstrated in certain cases of plague by Zabolotny, the test is of little or no value in diagnosis, as the reaction appears late in the disease, and in the most severe forms of the disease the patient dies before the reaction could be expected. The technical difficulties in the way of securing a satisfactory emulsion or broth culture for performing the test are considerable (Klein). A dilution of 1 : 20 with a time-limit of half an hour may be used.

Agglutination Reaction in Cholera—In cholera, apart from the historical interest and as a means of identifying the vibrio, the test is of small value. The reaction persists for a considerable time, and may be of use in determining whether a person has suffered from genuine asiatic cholera or as a means of tracing the source of an outbreak.

Agglutination Reaction in Tuberculosis.—Arloing and Courmont, after surmounting the difficulties of obtaining suitable cultures for the purpose, were able to apply this test for diagnostic purposes.

In low dilutions, 1 : 10, a reaction was present in 75 per cent of cases of pulmonary tuberculosis, and in about the same proportion of other forms of tuberculosis. These results have not been confirmed by Dr. Horton-Smith, Armitt, and others. Eisenberg and Keller, using serum from post-mortem subjects, obtained 70 per cent of positive results in non-tuberculous subjects.

Agglutination Reaction in Pneumococcal Infection.—Jehle states that the reaction is very constant, and of some value for use in pneumococcal infections. The culture used must be virulent. The reaction occurs early, especially in children. The test is sometimes performed by growing the organism in serum, a control preparation with normal serum being made at the same time (Eyre and Washbourn).

Agglutination Reaction in Streptococcal Infection.—The serum of animals immunised against any strain of streptococcus is capable of agglutinating that strain in high dilutions. Moser and Pirquet found that streptococci from a case of scarlet fever were agglutinated by the serum of a horse immunised against streptococci from the same source in dilutions up to 1-4000. With the blood- and body-fluids of patients suffering from small-pox, De Waele and Lugg were able to cause agglutination of the strepto-cocci, so constantly found in that disease, even in dilutions of 1-800. Immune sera from other sources had no such effect. Aronson and others believe that all streptococci may react to serum from a single source. From these and many other researches it appears that no clinical value can be attached to the test in the various forms of streptococcal infection, nor would it appear probable that such can be the case till some agreement has been arrived at as to the classification of streptococci by the help of this test or in some other way.

The reaction has also been described as occurring in glanders, in relapsing fever, and other conditions. A full account is given by Kolle and Wassermann.

The Opsonic Property of the Serum.—Drs. Wright and Douglas in two recent papers have drawn attention to the part played by the blood-fluids in connexion with phagocytosis. Using Leishman's method for measuring phagocytosis, equal volumes of a bacterial suspension and of blood are measured in a pipette, thoroughly mixed, placed on a slide, and covered with a cover-glass. The preparation is then allowed to remain for fifteen minutes in an incubator at 37° C. At the end of this time the cover-glass is slid off, the slide fixed and stained. The number of bacteria ingested by the polymorphonuclear cells is counted and divided by the number of cells. The result found in the blood under examination is compared with a control specimen prepared with normal blood. They modified this method by making the mixture in capillary pipettes, incubating it in this condition, and making the film after incubation. Further, by citrating the blood (1 per cent citrate of soda in salt solution) they were enabled to obtain the plasma and the leucocytes separately, by pipetting, after centrifugalisation. They demonstrated that "the phagocytosis, which occurs when staphylococcus pyogenes aureus is added to human blood, depends on certain substances in the blood which exert a specific action on the bacteria." To this substance they gave the name of Opsonin. They further showed in the second paper that in patients subjected to staphylococcus vaccination the increased phagocytosis, which is associated with the increased condition of immunisation as the result of this procedure, is dependent not on the corpuscles but on the opsonins in the plasma or serum. They found after heating the serum to 65° C. for ten minutes that though they remained unaltered the leucocytes had lost their power of phagocytosis almost entirely, but if the unheated serum were mixed with the bacterial emulsion and allowed to remain at 37° C. for fifteen minutes, and then heated, phagocytosis would take place. This power of the unheated

serum to prepare the bacteria and render them more acceptable to the phagocytes, they found present in the blood in many conditions. The organisms of plague, Malta fever, pneumonia, dysentery, and typhoid, among others, are influenced by this body, but diphtheria bacilli remained uninfluenced. This is not the place to deal with the important bearings which these facts have on immunity or on phagocytosis, but the property may afford a method of testing the varying resistance of patients in the course of infections, and provide a standard for judging the effect of treatment in certain cases. At present the results are too few to allow of any positive statement being made.

The Coagulation-Time.—Dr. Wright has drawn attention to many conditions in which coagulation of the blood outside the body is delayed. In hæmophilia, urticaria, and persons of a lymphatic habit coagulation may be delayed far beyond the normal limit. Alcohol and a restricted amount of solid food diminished the coagulability. A restricted ingestion of fluid, or an excess of carbonic acid in the blood, on the other hand, increased the coagulability. He points out the importance of these facts in their bearing on the treatment of aneurysm, urticaria, hæmophilia, and other conditions, as well as the use of the determination in estimating the effect of treatment.

Notwithstanding the researches of Dr. Wright and others, the determination of the coagulation-time has not yet entered greatly into the routine clinical examination of the blood, partly because most of the methods employed are too inaccurate. Dr. Wright's own instrument (Fig. 63), which is the best, consists of a central vessel, which is filled with water at the temperature of the body. Round it is a leather covering containing nine pockets, one of which holds a thermometer, the others a capillary tube each (*a*, Fig. 63). At regular intervals the capillary tubes are partly filled with blood and replaced in the pockets. After one or two minutes attempts are made to blow out the blood from one of the pipettes, and this is repeated at intervals with the tubes in turn till a tube is tried in which the attempt fails. The time of withdrawal of the blood in this tube being known, the coagulation-time is calculated. The normal time is about three or four minutes. The temperature of the heating vessel must be carefully maintained. Comparative results, especially by the same observer, are of much more value than isolated estimations.

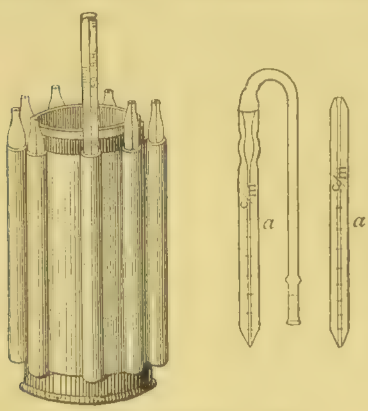


Fig. 63.—Wright's Coagulometer.

The Alkalinity of the Blood.—Methods have been devised by Löwy, Kraus, Wright, Schultz-Schultzenstein, and others whereby the degree of alkalescence of the blood or of the plasma may be estimated. In Löwy's method laked blood is used; in Kraus's, defibrinated blood: in

Wright's, serum; and the degree of *alkalinity determined by titration.* The results obtained are obviously not comparable, but comparative results may be obtained with any one. The clinical value of the test, however performed, is at present doubtful. It has been shown that changes in the degree of alkalinity in the blood occur in many conditions, but though the facts ascertained are of considerable interest from the scientific point of view, no indications, or but very few, are afforded by them in individual cases for treatment or diagnosis. With a larger number of observations on record this position may be altered. The variation is nearly always in the direction of a decrease of the degree of the alkalinity, though Dr. Copeman has recorded an increase in chlorosis. The alkalinity of the blood has been found diminished in carcinoma, in many acute specific fevers, in cirrhosis of the liver, uræmia, osteomalacia, and in diabetic coma. It is, of course, intimately connected with acid intoxication or acidosis (*vide* p. 543).

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J. H. D.

INFLAMMATION[1]

By J. G. Adami, M.A., M.D., F.R.S

PART I.—A General Survey of the Process of Inflammation

Chapter I.—Introduction

Definition of Inflammation.—It is usual to begin the description of a morbid process by defining that process. In the case of inflammation, however, we have to deal with a process so complex, so modified by modifications of the many factors involved, and so variable in its manifestations according to the variety of its causes and the region of incidence, that the attempt to define it has proved a pitfall to pathologist after pathologist; moreover, to advance a definition of the process at the begin-

[1] The following article is an attempt to bring into order the very numerous recent researches upon the inflammatory process, and to show whither they appear to tend. It in no wise pretends to be a complete treatise of the development of our knowledge of the subject; space alone forbids that I should trace the whole history. I would therefore strongly urge that, as a corrective, other works be consulted in which the earlier theories are treated at length. Sir J. Burdon-Sanderson, in Holmes' *System of Surgery*, gives a very good introduction and history of our subject. The bibliography contains other general articles which may, with benefit, be consulted.

ning of this article in terms differing to any considerable extent from those employed by previous writers, would demand a criticism of the many previous attempts; and in order that the definition put forward be duly supported, would necessitate an essay covering the whole field about to be traversed.

Use of the Name.—Yet, in the meantime, inasmuch as divergent views are held of the limitations of the use of the name inflammation, a few words of introduction are advisable.

Two courses are before us: either to employ the name strictly in accordance with the primitive definition, and thus only to include as cases of inflammation those states in which there are present redness, swelling, heat, and pain, rigidly excluding all cases in which these cardinal symptoms are not present; or, on the other hand, departing from tradition, to include as inflammations all those morbid processes which seem to have a cause and progress inseparable from and merging into the cause and progress of the state characterised by the classical symptoms. The first course is impossible; it is as though one were to declare that red phosphorus is not phosphorus because in externals generally it does not agree with the definition of the yellow form made years before the allotropic modification was discovered. We are now well agreed that of the classical symptoms, one, two, or three may be unrecognisable, and in fact absent; and yet the condition of inflammation be undoubtedly present.[1]

The second is the only possible course, that, namely, which associates all those states which under suitable conditions may result in the production of the four classical symptoms, and, moreover, originate from a common cause. Holding this view, it will in the meantime be well for me, in order to afford a starting-point for the description and discussion of the subject, to select from the many definitions one which is based not on symptomatology, but upon etiology, and indicates a common origin for all cases of inflammation. I would select that which in this country has received the most cordial support, the definition given by Sir J. Burdon-Sanderson (1) in his well-known article in Holmes' *System of Surgery*: "The process of inflammation is the succession of changes which occurs in a living tissue when it is injured, provided that the injury is not of such a degree as at once to destroy its structure and vitality." This definition includes too much. The hæmorrhage that occurs in the liver when it is injured, and the changes that there occur in the extravasated red corpuscles, are scarcely to be classed among inflammatory phenomena; the atrophic changes which occur in the retina, when through injury it becomes detached, are due mainly to malposition

[1] A course allied to this has found favour of late years among some surgical pathologists, who, with Hüter (2), would limit the use of the term to those cases and those only in which the classical symptoms, or the majority thereof, are present and associated with suppuration,—they urge with Zahn (3) that inflammation only occurs when pyogenetic micro-organisms are present, and state that when a wound heals aseptically it heals without inflammation. This modified course is equally impossible; pyogenesis must not be confounded with inflammation.

and disuse rather than to the primary trauma. Grawitz (4) has put forward a definition based upon the same fundamental conception, but so worded as to exclude largely, if not wholly, the above objections; for, as regards the second, it may justly be urged that atrophic changes are not reactive, but due to lack of reaction. Inflammation, he holds, is the reaction of irritated and damaged tissues which still retain vitality. Either of these definitions has this great advantage, that, stating the cause, it clearly recognises inflammation as a process and not as a state. The manifestations of this process under favourable conditions—where the region injured is a loose and vascular tissue, and where the injury is sufficiently severe or extensive—are redness, swelling, heat, and pain: redness from the congestion of the vessels; swelling from the exudation of fluid and corpuscles from the congested vessels; heat from the increased amount of blood in the region, and pain from the pressure upon and irritation of the terminations of the nerves in the region. To these four symptoms may be added a fifth, disturbance of function brought about by this departure from the normal condition of the region. Under unfavourable conditions—where the region injured is dense or less vascular, or where the injury is less severe—one or all of these symptoms may seem wanting; nevertheless a minute examination of the tissues will show the same succession of changes as in the former case.

Chapter 2.—The Comparative Pathology of Inflammation

Accepting, then, this working definition, in order to arrive at a due comprehension of the succession of changes which we take to constitute the inflammatory process, it will be well with Metchnikoff [1] (5) to institute a series of observations upon the reaction to injury exhibited throughout the animal kingdom from the lowest forms upwards to man. By this means we shall be enabled to determine what factors in the reactive process are from their constancy of primary importance; what are common and essential, and what are superadded in the higher animals.

The Response to Injury among the Protozoa.—Beginning our study with the lowest and simplest forms of life—forms so lowly that they have been regarded both as animals and as plants—we find even here phenomena accompanying the reaction to injury which throw light upon the inflammatory process as seen in the higher animals. Taking as an example the amœba, we find, in the first place, that the nucleus plays an important part in this reaction. If, as Metchnikoff has shown, one of the larger amœbæ be cut in two, the region of injury becomes rapidly

[1] The succeeding paragraphs are of necessity very largely an epitome of sundry portions of Metchnikoff's most pregnant work upon the comparative pathology of inflammation. By comparing them with the work in question, it will, however, be seen that they depart from it in several points; more especially in dwelling upon the extracellular activity of the wandering cells, and in bringing more prominently forward the response to injury on the part of the fixed cells.

indistinguishable—the protoplasm of each moiety closes up, leaving no mark or scar: but of the two parts that which retains the nucleus grows and proliferates; the other disintegrates in a longer or shorter time. Or injury may induce changes in the protoplasm of the entire amœba: thus Miss Greenwood (6) points out that, without necessarily bringing about death, the interrupted current or an aqueous solution of thymol leads to a process of exudation or extrusion of clear hyaline spheres, or of spheres holding crystals and granules, from the surface of the organism—a process resembling that occasionally seen in the cells of an inflammatory area in higher animals. Nor is this all; apart from changes in the structure of these unicellular animals, differences may be seen in the behaviour of amœbæ towards foreign bodies. It would seem, according to Le Dantec (7), that amœbæ ingest non-irritating foreign substances indifferently, provided they be sufficiently small. Around each particle so ingested a vacuole is formed, and the fluid in this becomes increasingly acid, and at the same time digestive. Krukenberg (8), Reinke, and Miss Greenwood have conclusively proved these and similar food vacuoles in the amœba and other Protozoa to contain a pepsin or digestive ferment, which, as Le Dantec has shown by very delicate tests, exerts its action in an acid medium (the general protoplasm of the cell-body being alkaline); this digestive process leads to the solution of food-stuffs, preparing them to be taken up by the protoplasm of the organism. If the foreign substances be incapable of digestion they are sooner or later extruded. It is by this formation of digestive vacuoles that the amœba acts upon and destroys bacteria, diatoms, and other microbes ingested by it. There are, however, microbic forms around which it would seem that no proper vacuolation is developed, or if developed, the acid digestive fluid is neutralised by substances discharged from the parasites; where this is the case, instead of destruction there is continuance of vitality and actual multiplication of the invading or parasitic form, leading to the eventual death of the amœba. Metchnikoff has observed this chain of events in one of the amœbæ which ingests and becomes the host of a minute rounded form, the Microsphæra. Phenomena of like nature may be observed among the ciliate and flagellate infusoria. Here it is worthy of note that bacteria, which, as we shall see, are the main causes of inflammation in higher animals, are in these lowly forms an important, if not essential, source of nutrition. So far it has not been found possible to gain pure cultures of the amœbæ: in other words, they are unable to obtain adequate nourishment from the various media of the laboratory. It has been found, however, by Frosch (9), Mouton (10), and others (11), that if certain of the commoner forms be isolated, placed in a suspension of a pure culture of the bacillus coli, or certain other species of bacteria, and then be "sown" upon the surface of a tube of sterilised agar broth, active growth and multiplication ensue, the bacilli being taken up and used as food. While these phenomena may primarily be regarded as the method employed by the Protozoa for the assimilation of food-stuffs, they also are clearly the means whereby the Protozoa defend themselves against

living organisms which have gained entrance into them, and thus form the reaction to possible injury; for when in certain cases the means of defence are overcome, the parasitic organisms gain the upper hand and lead to death.

There is yet another reaction to injurious influences exhibited by the Protozoa into which it is necessary to enter at some length. This is exhibited by the amœba, but can be and has been most fully investigated in the myxomycetes—multicellular forms which can with equal propriety be classed as animals or plants, although usually they are included among the latter. These organisms form large plasmodia (masses of protoplasm, that is), in which, under ordinary conditions, the nuclei are the only indication of the individual cells which by their fusion have formed the masses. They are to be met with in leaf mould, and on the surface of moist decaying wood, over which they creep with an amœboid movement; and inasmuch as they may attain great size—some species attaining twelve inches or more in length—they form admirable material for biological study.

Twenty years ago Stahl (12), investigating one of these myxomycetes (the *Æthalium septicum*, an organism found in tan-pits), showed that if placed upon a moistened surface close to a drop of infusion of oak-bark, the plasmodium moved actively towards and into the infusion; if placed similarly near to a solution of glucose (0·5 per cent) it moved with equal rapidity away, and so also in the case of solutions of various salts. These observations of Stahl were (if we except Engelmann's observations in 1881 upon the tendency of sundry bacteria to remove from regions poor in oxygen to those where oxygen is present in abundance) the first of a series of observations upon the attraction and repulsion of plants and portions of plants by chemical substances. To this property Pfeffer (13), who has made the fullest series of studies upon it, has given the name of chemiotaxis, in place of Stahl's narrower "trophotropism"; and one speaks of a positive or a negative chemiotaxis according to the attraction or repulsion exerted. If, as Metchnikoff has pointed out, the advancing edge of one of these plasmodia (of Physarum) be injured by cauterisation, the region of injury dies; the protoplasmic currents, which had been advancing, reverse themselves abruptly, and within an hour the plasmodium has moved away, leaving the debris of the destroyed region behind. These experiments are so simple, and the results obtained seem so natural, that it may be asked whether it be worth while to attach a name to this property of living matter. Yet the name is in itself an aid to bearing these properties in mind; and, as will be pointed out later, the recognition of them is of material help in solving certain of the difficulties that present themselves in the study of inflammation in the higher animals. Among these myxomycetes another point can be made out. Stahl observed that the plasmodium of Fuligo, which at first moves away from a two per cent solution of common salt, will after a time (more especially if it has suffered from lack of water) adapt itself to the solution, advancing its pseudopodia or protoplasmic processes

into it. With other myxomycetes the same *adaptation* has been observed. That is to say, by use or adaptation a negative may be transformed into a positive chemiotaxis. To this change I shall have occasion to revert.

A similar, and suggestive, series of adaptations has been noted by Musgrave and Clegg (14) in their studies upon amœbæ. They note that these in their natural environment—the pathogenetic forms in the large intestine, for example—are selective, feeding upon only one of the many surrounding species of bacteria. Away from that natural environment they grow abundantly upon the surface of agar tubes in association with this one form. By the gradual addition of pure cultures of another bacillus, with which, at first, growth is not possible (the amœbæ not taking them up, and starving as a consequence), the amœbæ first become accustomed to this foreign form, then take up occasional individuals, until eventually they will feed upon and grow in a pure culture of the second form, in the total absence of members of the first species. Nay, more, these observers noted that one particular amœba, isolated from Manila tap-water, and grown in conjunction with a species of bacteria present in that water, set up abscess-formation when inoculated with it into the liver of animals of the laboratory: from such an abscess growths of the amœba could be obtained in association with the microbes in question. But if passage were made through two more animals of the same species, setting up in them liver abscesses, it was found impossible to gain growths in like manner. The amœbæ were there, but growth in the tissues had changed their habits. They had clearly accustomed themselves to a wholly different form of food—presumably to cell-products of the organism; a point which throws light upon the frequent occurrence of tropical abscesses of the liver, in which amœbæ are present without associated bacteria.

The Response to Injury among the Metazoa.—Passing from the Protozoa to the Metazoa, we reach immediately (or almost immediately) a series of beings in which the division of labour among the cells has led to the development of three cell-layers—an outer ectoderm, an inner endoderm, and an intermediate layer of mesoderm. Even in the very lowest forms among the Metazoa it is noticeable that of these three layers there is one, the mesoderm, whose cells have the especial function of reacting when any irritant or injurious stimulation is applied to the organism. Taking what are perhaps the simplest forms in which to observe the relationship and properties of these layers, Metchnikoff has studied these results of injury in the larval forms of Astropecten and other echinoderms. At one well-recognisable stage these larvæ resemble little more than the gastrula stage of the embryologist; the endoderm or hypoblast appears as a cul-de-sac—an invagination of the ectoderm or epiblast—while the mesoderm is represented by amœboid cells, budded off from the endoderm, lying or floating in the semiliquid substance filling the general body-

cavity.[1] The ectoderm is so delicate that any sharp substance can readily penetrate into the body-cavity; and, when this happens, it is noticeable that the wandering mesodermal cells make their way to the foreign body, attach themselves to it, and fuse into plasmodial masses, thus forming a wall, as it were, around the invading substance, and cutting it off from the general body system. Here, then, in an organism possessing neither nervous nor vascular system, the reaction to injury, when that injury has not been sufficiently intense to cause destruction of the outer layer of cells, is simply and solely confined to the wandering cells of the body; there is no effusion of fluid; there is not necessarily phagocytosis

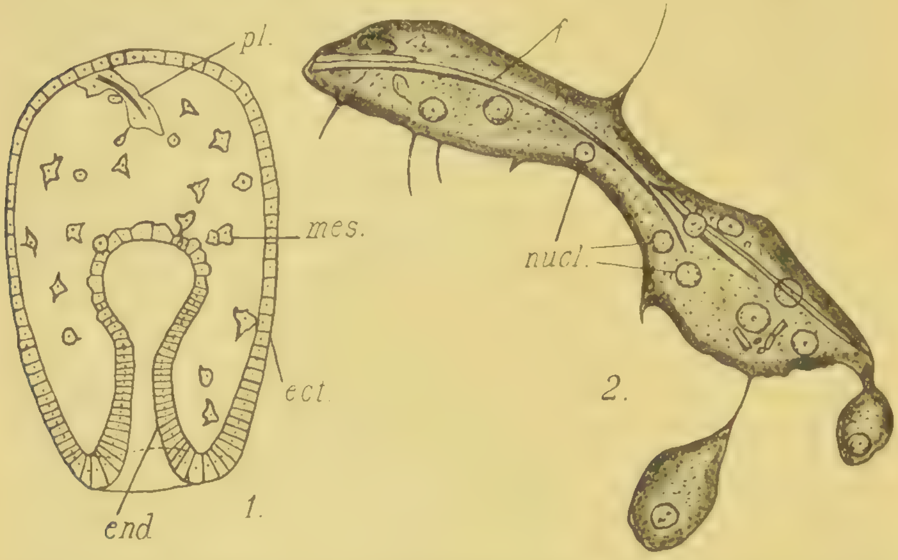

FIG. 64.—1. *Larva of Astropecten*, modified from Metchnikoff to show *end*, endoderm; *ect*, ectoderm; *mes*, mesodermal wandering cells; *pl*, plasmodium of mesodermal wandering cells formed around foreign body which has punctured the endoderm. 2. The *Plasmodium*, from the same larva, highly magnified; *nucl*, nuclei of the fused wandering cells; *f*, spicules of foreign matter around which the cells have collected.

on the part of these cells; any digestive and destructive action on their part—any attempt in this way to remove the foreign body—must then be by excretion, *by extracellular action.* At the same time, this fusion of the cells and formation of a plasmodium around foreign substances of greater diameter than the individual mesodermal cells may be looked upon as a mechanism whereby the equivalent of intracellular digestion is gained. But, as among these low forms cases occur in which, without the formation of plasmodia, the cells perform their destructive action

[1] As indicating the earliest stage of these wandering cells it is noteworthy, as MacBride (15) has pointed out, that in the gastrula of *Echinus esculentus* two forms of wandering mesenchyme cells are present in the body-cavity: one obviously stellate, and attached to other similar cells and to the body-wall by long processes; the other, rounded forms (amœbocytes), which, while appearing free, are connected with neighbouring cells and the body-wall by means of excessively fine threads, along which they appear to travel. The cells at first are therefore only relatively free.

upon bodies of larger size than themselves we do not lack examples of what must be considered as excretory destructive powers on their part. That these cells in the echinoderms are also capable of destroying minute foreign bodies by intracellular action, that is, by phagocytosis, has been demonstrated in the larger transparent larval form known as *Bipinnaria Asterigera*; on introducing bacteria under its ectoderm the mesodermal cells are seen to approach, and by their long pseudopodia to adhere to and ingest the still living motile bacteria, which are rapidly digested.

Besides this reaction to injury on the part of the mesodermal cells, a further response is exhibited to a remarkable degree among the lower Metazoa—I refer to the great power of regeneration of lost parts, of cell-proliferation leading to the reproduction of destroyed regions. This power is best seen in the classical example of the Hydra, which may be cut into many pieces, each one of which is capable of growing, so that in a relatively short time it becomes a fully formed individual. It is interesting to note in relation to the frequent tendency towards hyperplasia and excessive growth following upon injury in the higher animals, that among low forms, such as Hydra and Cerianthus, the same tendency is yet more strongly marked. Thus, as J. Loeb (16) points out, if an incision be made in the stem of a Hydra, a whole new oral pole, provided with tentacles, will branch out from the region of cell-destruction. In the actinian Cerianthus the process is not quite so extensive; yet from the lower lip of the lateral incision a set of tentacles develops in all respects similar to those around the mouth.

Ascending to the Worms, we find that the protective agency devolves upon mesodermal cells suspended in the perivisceral fluid, and again forming the peritoneal endothelium. We arrive, that is to say, at a stage in which a lymphatic system may be said to be present; for the spaces in which the free corpuscles lie are strictly homologous to the lymph-containing spaces of the vertebrate organism, and these corpuscles may be regarded as lymph-corpuscles; the peritoneal endothelium corresponds with the mesodermal peritoneal endothelium of vertebrata. It is the fixed as well as the wandering cells that take part in the process.

Among the Annelids the process of reaction to injury may be well followed in the earthworm by studying the sequence of changes that occurs around the gregarines which infest the male genital organs. While these parasites are active they prevent by their movements the adhesion of the wandering cells; but so soon as they pass into the resting stage antecedent to spore-formation, the cells form a thick mass around them. The parasite on its part forms a thick cyst-wall; nevertheless, it may not unfrequently be observed that, despite this protection, the parasite changes its appearance under the action of the surrounding plasmodium, and in fact is killed. While this is happening no change could be detected by Metchnikoff in the neighbouring blood-vessels; these appear to remain completely inactive: no exudation is noticeable nor any recognisable change in volume. The nature of the injury inflicted without doubt influences the character of the reactive process.

Thus causing direct injury, either by passing a thread through the body, or by cautery, Messing (17) found that in the earthworm and leech regenerative changes are both more pronounced and of more rapid development than is the accumulation of wandering cells. In six hours the injured epithelium might show definite signs of regeneration, while at this period but few mesodermal cells had collected.

While among the Worms a well-developed and closed vascular system is not infrequently present, in other animal forms, which in most respects present a much more complex and advanced development, namely, in the Molluscs, Arthropods, and Tunicates, this is not the case. In these the blood pours from the tubular heart sooner or later into the lacunæ of the general body-cavity; and whether veins and capillaries (*i.e.* finer vessels lined with endothelium) be absent (as is most usual), or present (as in the Cephalopods), the blood is sucked back from the body-cavity into the heart. This incomplete circulation, interesting as it is in connexion with the development of the vertebrate circulation, is interesting also because its incompleteness in these large and widespread classes of animals prevents reaction to injury from being associated with vascular changes. The blood in these animals, circulating through the ramifications of the body-cavity, is evidently a mesodermal fluid, if it may be so termed. Its corpuscles are clearly mesodermal; and without going into full details as to the properties of these corpuscles, it may be said that they represent an interesting series of stages in the subdivision of labour. For example, as Mr. Hardy (18) has shown us in a low form of crustacean like Daphnia (the water-flea), but one form of cell is present, whereas in the highly developed Astacus (the cray-fish), there are three distinct forms of leucocytes (no red corpuscles being present), each of which appears to have distinct functions. The one form in Daphnia has the property of taking up fat globules and food particles from the alimentary tract, foreign particles, such as granules of carmine or Indian ink, and the spores of parasites (Monospora, Metchnikoff); it is granulated, containing minute spherules which stain with basic aniline dyes (basophil granules), and in certain circumstances it may be seen to explode with lightning-like rapidity. In the higher Astacus there are in the circulating hæmal fluid two varieties of cells: one is extraordinarily explosive; when removed from the body-cavity it gives off fine blebs or vesicles of its substance with such rapidity that, unless the greatest care be taken, nothing is seen of the cell save its nucleus; this form is phagocytic: the other form is far more stable, and is loaded with large spherules which have a great affinity for acid dyes—they are eosinophilous—may be actively extruded, and undergo decomposition; these cells never act as phagocytes. The third form, with basophil granules, is rarely found in the blood, and then only as the result of special stimuli; but it is present in considerable numbers in the peculiar tissue which forms a sheath around certain of the arteries—Haeckel's "Zellgewebe"; this form is phagocytic, and can be seen to contain globules of ingested fat.

Metchnikoff (19) demonstrated, in his most remarkable study upon a disease of Daphnia caused by the entry of the spores of a yeast-

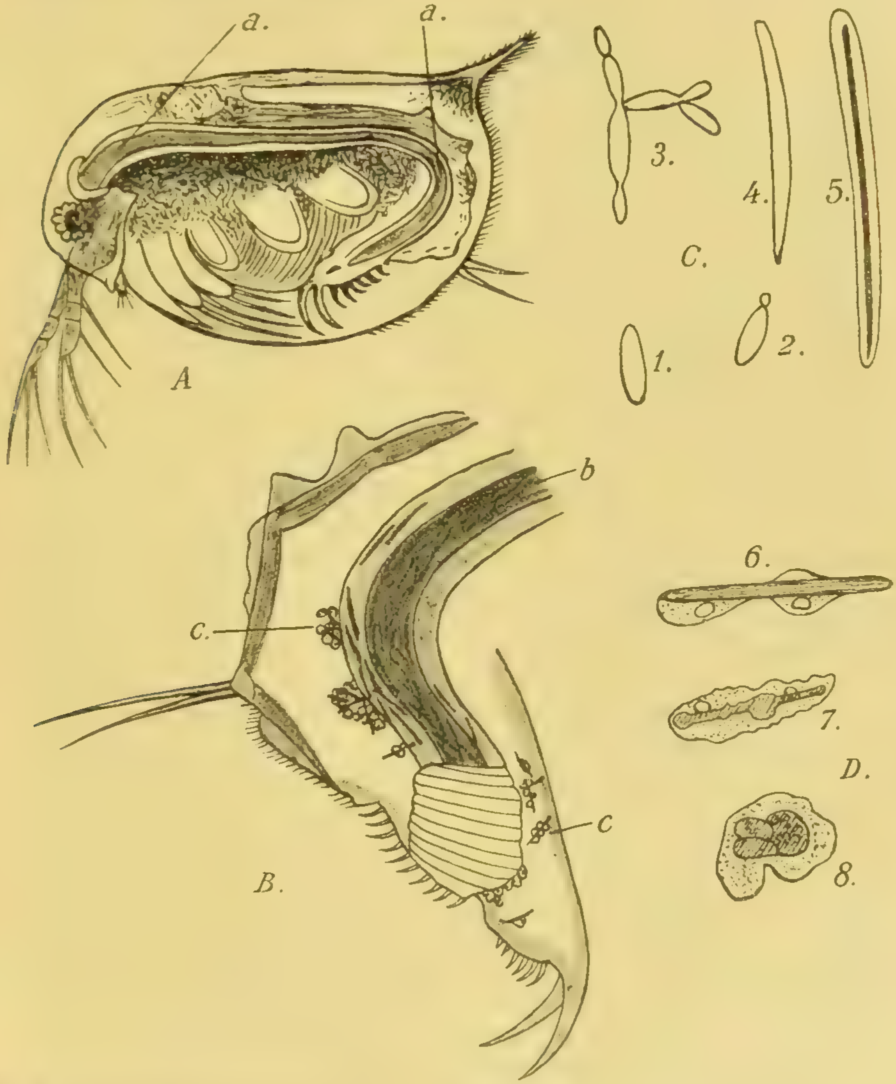

FIG. 5.—*A*, A *Daphnia* (water-flea) invaded by the parasitic yeast, *Monospora*. The deep shading, more particularly below the intestinal canal (*a*), is due to the mass of spores which have penetrated into the body-cavity. *B*, Anal end of an infected Daphnia. The elongated spores are to be seen in the lumen of the gut (*b*), in the walls of the same, and others which have penetrated the walls and have entered the body-cavity are seen with leucocytes attached (*c.c*). *C*, Stages in the development of Monospora. 1. Individual elongate oval torula. 2. A torula budding. 3. Do., later stage. 4. Much elongated torula prior to spore-formation. 5. Torula with contained spore. *D*, Stages in the destruction of the spores. 6. Spore with two leucocytes attached. 7, 8, Later stages of erosion and digestion.—METCHNIKOFF.

like organism (the Monospora) into its body-cavity, that its one form of leucocyte can be seen to react swiftly towards the spores: the cells approach them, form a plasmodium around, and eventually digest and

destroy them. If, on the other hand, in consequence of their great numbers or the relative paucity of the leucocytes, certain of the spores be not attacked and develop uninterruptedly into mature torulæ, the leucocytes show no tendency to approach them—in fact, their neighbourhood leads to the explosion of the leucocytes—and the torulæ, multiplying, lead to the death of the organism. Often, again, brown eschars may be recognised upon the transparent carapace of a Daphnia, due to injuries by other individuals; beneath these scars are to be found masses of leucocytes which remain in the region of injury until the cells of the tissue have proliferated, and there is complete union and repair.

In addition, then, to the immediate reparative and protective reaction of the leucocytes, there is exhibited among the higher invertebrata a later reaction in the shape of proliferation of the fixed cells; nay, at times the proliferative and regenerative process may be the more pronounced. This proliferation can be very great; and cells of all forms, whether of hypo-, meso-, or epiblastic origin, and tissues so highly developed as the muscular and nervous, may participate in it. In illustration of the ample power of tissue-reproduction after injury possessed by these animals, I need but mention the trite examples of the reproduction of the hinder segments of divided worms, and in crustaceans the restoration of injured and cast-off claws and appendages.

Many more instances might be given to show that the reaction to injury remains essentially a reaction on the part of the wandering and fixed mesoblastic cells of the organism, followed in sundry cases by proliferation of the fixed epi-, meso-, and hypoblastic cells, and by repair where these have been destroyed. Although these arthropods, molluscs, and tunicates have a vascular system, yet, since this is open, changes in it, if they occur, could scarcely modify the inflammatory process.

The Response to Injury among the Vertebrata.—If now we pass to the vertebrates, the picture presented is far more complex; not only do these present a highly developed nervous system, but the blood is enclosed in a complete vascular system. It is but just to call attention again to the fact that many authorities deny that up to this point we are justified in speaking of inflammation, urging that inflammation can only be said to be present when there is "flaming," *i.e.* increased redness and heat, due to increased blood-supply, that is to say, to vascular changes. While this position is etymologically correct we cannot accept it, because, as will be pointed out in the next chapter but one, we find that where this "flaming" is present, the process, nevertheless, in essence, is identical with that in the lower animals devoid of a complete vascular system.

Chapter 3.—The Experimental Production of Inflammation in Non-Vascular Areas

Let us begin with the succession of changes that occurs in the simplest case, namely, *in a non-vascular area, in one of the lowest vertebrate*

forms—for instance, in the embryonic Axolotl ten to fifteen days old; let us curarise it, and apply a minute crystal of silver nitrate to the side of its flattened transparent tail-fin, washing away the remains of the crystal with salt solution; or again, we may pass into the tail a small needle filled with finely powdered carmine. By either procedure a certain number of cells is destroyed. The neighbourhood of the injury now becomes swollen, and the surrounding cells tumefied, vacuolated, and less refractile. This is the *first stage*—that of injury and modification of the surrounding tissue. In a little time a few wandering cells (leucocytes) approach the injured region; by the next day these are present in fair numbers, and can be seen to have taken up the particles of carmine or debris of the destroyed tissue. This is the *second stage*—that of immigration of leucocytes. There are no vessels in the transparent fin of these young axolotls, no dilatation of those nearest to the fin, and no diapedesis. All the leucocytes that pass to the part are pre-existing wandering cells of the connective tissue,—a point of some little importance in connexion with the origin of certain of the pus-cells in the suppurative process of higher animals. The *third stage* is that of repair, of proliferation of the injured epithelium, return of the fixed cells of the tissue to their previous state, and emigration of the wandering cells.

A very similar progress of events occurs if the experiment be repeated upon the tail-fin of the young newt. The same rapid alteration in the large branched connective-tissue cells (which become vacuolated as their long processes are drawn in and shortened), and the same immigration of motile cells from the surrounding connective tissue are to be seen; but here we now find the earliest evidence of vascular participation, for, according to Metchnikoff, complete arrest of the circulation may occur in the nearest vascular loop. By the next day the parts have returned to the normal condition.

If from these cases we pass to mild inflammatory disturbances affecting the non-vascular regions of animals far higher in the scale, we again discover a like process of events. For this purpose *the cornea* affords an excellent opportunity; in health it is absolutely non-vascular, perfectly transparent, and so thin that it can readily be examined microscopically. The cornea of mammalia, and indeed of vertebrates in general, is formed of fibres which run in layers parallel to the surface. These fibres, while roughly arranged side by side and parallel to one another in any given layer, are placed at an angle to the fibres of the layers above and below. Although free from blood-vessels the cornea is far from being devoid of channels along which lymph freely passes. Between the several layers there exist spaces in which lie the flattened connective-tissue cells of the organ; and, by means of numerous fine channels, these spaces around the cells are connected with similar spaces lying in front, behind, and at the sides. Through this rich anastomosis of channels there is a free flow of lymph. These channels are really continuations of the body-cavity of the animal; they represent, and in fact play the same part as the single body-cavity of such a simple form as the larva of

Astropecten, while the cells lying in the spaces are mesoblastic cells which have become fixed.

Few studies are better calculated to impress the investigator with a sense of the depth of the well at the bottom of which truth lies, than a research into the abundant literature dealing with observations upon the stages of the inflammatory process as it occurs in the cornea, and with the deductions therefrom. The adherents to successive forms of inflammatory belief have found in experiments upon this simple tissue ample support for their particular creeds. Selecting from the many observations those which have stood the test of time, I will begin with the simplest, and pass on to those dealing with an increasing intensity of the inflammatory process.

If, as Senftleben (20) first pointed out, the centre of the cornea of a rabbit be washed with a strong solution of zinc chloride, then, in favourable cases, although the epithelial covering be gravely injured, there may be no actual rupture of the outer layers of the tissue. Such a cornea removed twenty-four hours later may show no sign of migration of leucocytes—no sign, again, of congestion of the vessels at the periphery. The only indications of injury and reaction may be the destruction of the corneal corpuscles immediately beneath the cauterised area, and the appearance of a zone surrounding this in which the corneal corpuscles appear enlarged, distinct, and tumefied. The process may continue and advance insensibly to repair without the intervention of leucocytes; the hypertrophying cells of the "granular" zone eventually undergoing karyokinesis, and thus by multiplication replacing the corpuscles destroyed. Here, then, necrosis and new growth of the fixed cells of the tissue are the only recognisable factors in the process of repair of injury. It must be confessed that the conditions permitting this simplest form of reaction are of rare occurrence; it is worthy of attention that they can exist. By a slight modification of the preceding conditions another factor may be brought into play. If, after cauterisation in the manner above described, a break be made into the cauterised surface; or if, again, without cauterisation, a little of the corneal tissue be removed, then in a few hours a small whitish opacity is to be noticed within the corneal tissue in the immediate neighbourhood of the break in the continuity, and upon examination this opacity is found to be due to a massing of small round cells. As there is at this moment no sign of proliferation of the connective-tissue cells of the cornea, these newly collected cells can only be leucocytes; and further examination of their properties proves them to be such: there is, however, no evidence of dilatation of the peripheral vessels, no indication of diapedesis through their walls. The leucocytes, therefore, can only have entered into the wound from the cornea itself and from the conjunctiva and the lacrimal fluid bathing it. In this experiment the inflammatory process is represented by destruction of tissue and immigration of leucocytes, followed by repair; neither the vascular nor the nervous system play any part in it. We are forced to the conclusion that the leucocytes have massed themselves in the injured

area purely on their own initiative; and that there must be an attraction, a chemiotaxis or chemiotropism, leading them actively to approach the region of cell-destruction.

Or we may proceed a step further. A fairly severe aseptic injury can be produced by cauterising the centre of the cornea. In thus treating the pigeon's cornea Goecke (21) noted that the wandering of cells towards the damaged area is first visible twelve hours after the injury, and then proceeds from the periphery. Obviously the wandering cells are white blood-corpuscles, and pass from the peripheral vessels. In twenty-four hours the process and the accumulation of round cells reach their climax. Some of the new-comers break up, others, according to Goecke, show signs of division. But soon these foreign cells commence to wander away, and at the end of thirty-six hours scarce any are left.

Turning to the fixed cells of the part, it is deserving of note that, before ever a leucocyte has reached the injured area, the corneal corpuscles, bordering upon the area of cauterisation, show evident signs of enlargement and growth. On the second day there are indications of active proliferation; and these newly formed corneal corpuscles behave exactly like certain white blood-corpuscles, from which they are indistinguishable. The vexed question of the relative part played by the wandering white corpuscles of the blood and wandering young connective-tissue cells will be touched upon later. It is, however, well to impress upon the reader that, at a certain stage, what we may term histogenous and hæmatogenous wandering cells are wholly indistinguishable by our present methods of study. The fight has been particularly bitter regarding these cells in connexion with this very subject of experimental keratitis.

The observations made upon these three more simple cases help us materially to understand the series of events which occur in more intense inflammation of the cornea, such as that produced by injuring the surface and causing the entrance into the injured region of a small quantity of a pure culture of the pyococcus aureus. This may be accomplished by injecting the culture into the centre of the healthy cornea by means of the needle of a Pravaz syringe (Jacobs) (22). The micrococci so introduced grow rapidly, the growth so extending along the lymph-spaces that a branched mass of the microbes is produced, having the spot of inoculation as centre. Around the growth as it extends may be seen a sharply marked area in which the corneal corpuscles show evidences of degeneration; the nuclei stain faintly, and the corpuscles, speaking generally, have a shrunken appearance. Here, again, the first effect of a microbic, as of a simple chemical injury, is to bring about degeneration of the fixed cells of the tissue. Within eighteen hours the zone of proliferating cocci and cell-degeneration is well marked; and now the second stage begins to be clearly manifest, namely, the determination of leucocytes to the seat of injury. Within twenty-four hours there is a dense packing of these corpuscles around the central degenerated area, and great numbers of leucocytes may be seen converging along the lymph-spaces from the periphery of the cornea. This is the second stage of the process, the first

stage of obvious reaction to the injury inflicted by the invading micro-organisms. If, as by Cohnheim[1] (23) in his original experiments upon the injury to the cornea, more careful examination be made into the stages of the determination of leucocytes, it can be seen that this determination is closely related to changes set up in the veins at the periphery of the cornea; they become more prominent, the region has a congested appearance, the smaller as well as the larger vessels are dilated, and there is abundant evidence that the leucocytes are passing out from the contained blood into the surrounding lymph-spaces. Indeed the accumulation of leucocytes shows itself first at the periphery of the cornea near the vessels, and gradually approaches the region of injury. Into the mechanism of this diapedesis, and into a fuller description of the changes that take place in the blood-current in these distended vessels, I shall enter later when discussing the changes in highly vascular regions. Suffice it to say here that no distinction can be made out between the behaviour of the leucocytes in the previous experiment, when they entered the wounded area from the external surface, and in this where the majority find their entrance from the blood; as in the previous case the part played was evidently active, so must it be here also. We cannot arrive at any other conclusion than that some attractive force leads to their determination towards the inflammatory focus. It is the polymorphonuclear leucocytes which at first most actively migrate. As Councilman (24) points out, in experimental pyococcic inflammation, as early as fifteen minutes after inoculation of the centre of the cornea a greater number than usual is seen in the conjunctiva. A more granular, more sluggishly amœboid form follows, most numerous in eighteen to twenty-four hours, while lymphocytes are not visible until the fourth day, and then do not so much pass out of the vessels as from the sheath of lymphoid tissue surrounding them. As we can easily show, by repeating the experiment, many of these leucocytes take up and contain numerous cocci, while other cocci remain free in the tissue-spaces. Many of the leucocytes degenerate and present a broken-down appearance; and, as at the same time an increasing area of the corneal tissue becomes disintegrated, an ulcer appears. According to the virulence of the culture and the reaction on the part of the organism, the process may now extend, a larger and larger portion of the corneal tissue becoming affected; or, on the other hand, there may be an arrest of the progress, the massing of the leucocytes preventing, as a barrier, the further extension of the micrococci into the lymph-spaces;[2] while at the same time there is an advance of newly formed capillary vessels into the previously non-vascular tissue. It is to be noticed that the blood-vessels at the periphery of the cornea are prominent and dilated, and from them fine new vessels with very delicate walls pass towards the injured region. At the same time many of the corneal corpuscles, outside

[1] There can be no question that Cohnheim in his experiments induced not a simple keratitis but one which in the absence of aseptic precautions rapidly became infective and suppurative.

[2] Into the details of this action I shall enter more fully later.

the area of destruction, can by appropriate staining be seen undergoing mitosis and proliferating. Thus the active repair of the tissue is initiated. The regenerative process is best observed in young animals by the use of caustics without causing a break in the continuity of the surface. Twelve hours after injury indications of cell-growth may be made out; in twenty-four hours mitoses are numerous, but occur only in the zone immediately surrounding the necrosed area. The corneal corpuscles become larger, their protoplasm more abundant; the cell-bodies stain more deeply; the

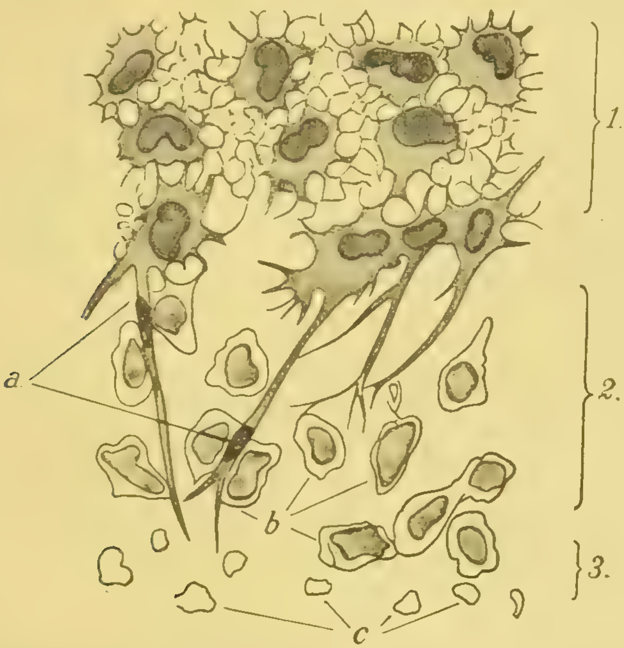

FIG. 66.—Mild grade of keratitis, commencing regeneration after forty-eight hours. 1. Peripheral zone of corneal corpuscles, showing enlargement with nuclear multiplication. 2. Zone of degenerating granular corneal cells (*b*). 3. More central area of cells destroyed and broken up by the action of the caustic (*c*). *a*, Processes from proliferating corneal cells with nuclei advancing into region of irritation and degeneration.—After SENFTLEBEN.

nuclei become more rounded and also more deeply stained; the cells give off long processes—always towards, never away from, the necrosed area, and with division of the nuclei the young nuclei make their way into those processes, and so into the dead tissue. In this way new typical corpuscles are formed in the course of the branches, which further show abundant cell-inclusions; in other words, the growing tissue-cells feed upon the migrated leucocytes.

CHAPTER 4.—THE EXPERIMENTAL PRODUCTION OF INFLAMMATION IN VASCULAR AREAS

From this study of inflammation, as it occurs in a region primarily devoid of blood-vessels, let us now pass on to the more complicated

process of inflammation in vascular areas; and, as in the previous case we considered an ascending or advancing series of reactive changes, so here let us begin with the slightest injury associated with the mildest reaction, and pass onward to states in which the inflammatory manifestations are more and more pronounced.

If an incision be made with a perfectly aseptic instrument into the skin, also rendered aseptic, and be so made as to divide the dermis and tissues immediately below, without at the same time injuring any large vessel, it is the common experience of modern surgeons that repair takes place with the minimal amount of change recognisable as inflammatory. Repair takes place indeed so rapidly that, if the divided structures have come or have been brought into immediate contact, there may be firm adhesion at the end of twenty-four hours. This is *primary union*, or union by first intention, which, rare in the old days, commonly occurs in this era of aseptic surgery. The full sequence of events in these cases cannot, it is true, be well determined by continuous microscopic examination; but if the rabbit or dog be employed, and tissues, wounded in the manner described, be removed and examined at successive short intervals, we see that the changes which occur are mainly, nay, almost entirely, related to the pre-existing cells of the part. The section divides a certain number of capillaries; but in the very act of division the divided walls are apparently brought together; and, partly by this means, partly by contraction, the lumina of these minute vessels become occluded, and the hæmorrhage into the wound is altogether inconsiderable. Within an hour after the operation it is evident to the naked eye of a careful observer that the immediate neighbourhood of the wound is reddened and tumefied, but only slightly; and, associated with this, there is a feeble exudation between the apposed surfaces. But the exudation is not great, and even within this first hour after the infliction of the wound there may be development of fibrin and coagulation of the exudate, leading to a provisional cicatrix cementing together the opposed surfaces. In this exudation, and in the tissues in the immediate neighbourhood, the leucocytes that have undergone diapedesis may be few and far between, and may scarcely attract attention. The reaction, then, on the part of the vessels and of the leucocytes is of the slightest. At times the dilatation of the vessels is more considerable, and with this there is a fair amount of oozing into the wound of a thin serum, which has little tendency to coagulate. Thus it has not been an infrequent experience of surgeons that if an extensive skin-flap be sewn up completely the amount of serum accumulating between the surfaces of the wound during the next few hours causes not a little tension and discomfort. If one or two of the stitches are cut and this serum allowed to drain away the parts unite forthwith. It has become the practice to make allowance for this serous oozing by not completely closing one end of such a wound, and inserting there temporarily a "drain" of sterilised gauze, so that this fluid escapes immediately and primary union is facilitated.

Study of sections in these cases shows that the main part is played by the pre-existing cells of the part; of these a certain number (not so many as might *à priori* be expected) are destroyed immediately, and show all the signs of disintegration; a number relatively large have been injured only, their nuclei remaining intact, though their processes or some portions of the cell-bodies have been cut through. It is difficult to determine these injuries in the small cells of the cutaneous tissues; they are better seen in the peritoneum when slight inflammatory changes have there been induced. It can, however, be made out that the cells in the immediate neighbourhood of the wound became enlarged, and, without showing signs of division, prolong themselves (that is to say, send out prolongations) into the region of the provisional fibrinous cicatrix. In this way, before the end of the second day, there may be a more or less complete replacement of the primary unorganised cementing substance by organised growing tissue,—formed, in the first place, by the interlacing of processes from the neighbouring cells; in the second, and later, by a multiplication of these cells, together with a development of new capillaries, few in number, which branch off from the slightly congested vessels in the neighbourhood. Thus in this case the process of repair is characteristically associated with hypertrophy and the new growth of the fixed cells of the tissue; while vascular changes, exudation, and leucocytosis are relatively little marked. I have, however, never come across a case in which they have been entirely absent, save when the section has been truly extra-vascular—that is to say, when it has not penetrated into the vascular region of the skin, and has affected only the epidermis and outermost layers of the dermis. In such cases the response to injury may show itself purely as a proliferation of the epithelial cells. As I have said, observations of this nature labour under the disadvantage that they must of necessity be discontinuous. I bring them in at this point, inasmuch as they represent the mildest condition of the inflammatory reaction. I have not personally observed this series of changes in tissues which permit of continued study under aseptic conditions; neither am I acquainted with any observations wholly fulfilling these conditions — made, that is to say, upon transparent vascular tissues subjected to the mildest aseptic injury and examined continuously under the microscope.

The response to injury in the cases just mentioned was of the slightest. Let us now pass on to cases in which it becomes more pronounced; and in order to continue the comparative study of inflammation I would first describe the series of *events in a highly vascular and transparent region* in a low vertebrate animal, namely, in the tadpole's tail. If this be injured, either by the application of a caustic or by the introduction of a foreign inert body into its substance, a definite advance upon what was recognisable in the case of the axolotl, for example, is to be made out. Here the tail is very vascular, the wandering cells in the connective tissue are very few in number, while the blood is fairly rich in leucocytes, which are small relatively to the

size of the vessels. The results of injury are a congestion of the vessels, noticeable within fifteen minutes, and a well-marked determination of leucocytes to the injured region. These cells, in the main, pass out from the vessels; the few leucocytes pre-existing in the tissue appear to play a very small part. Compared with the axolotl experiment this observation is of considerable interest. *Instead of a slight reaction slowly developing there is a rapid reaction*; instead of a slight accumulation of leucocytes there is a most pronounced accumulation. If there be any meaning in the determination of leucocytes to the region of injury, then evidently the active participation of the vessels of that region in the reactive process is fraught with benefit—it is a further important factor developed with the development and advance of the organism.

The fuller details of this vascular interference in the inflammatory process have been followed by many observers, among whom first and foremost was Cohnheim (23), and to this end the frog has supplied the most convenient means in regions at once vascular and fairly transparent, such as the web of the hind feet, the tongue, and the mesentery. Other observers passing higher in the scale of vertebrates have employed the mesentery of the cat, dog, and other mammalia. Suffice it to say that, with slight modifications due to local conditions in the tissue examined rather than to the animal selected, the process has been found to present the same features throughout the whole of the adult vertebrata, from the reptilia upwards. For general examination, perhaps, the best and simplest method of observing the succession of changes that follow injury of a vascular area is to be found in Coats' modification of Cohnheim's original experiment upon the frog's web (25). In order to reproduce as nearly as possible the conditions of an early wound, instead of employing a caustic or chemical irritant, a small portion of the cutaneous surface is nipped off—the section being just deep enough to pass through the cutaneous layers without causing hæmorrhage. For the experiment to proceed satisfactorily, it is necessary that the frog be curarised after having been pithed. The web of a small frog is so thin that the changes occurring in and around the vessels of the part can readily be followed even with a high power of the microscope.

The first change noticeable in the immediate neighbourhood of the injured membrane is a dilatation of the vessels, first of the arteries and then of the veins; and in this first phase there is a very evident acceleration of the blood-flow. At this early period the capillaries show little evidence of dilatation, but in the course of an hour expansion is readily distinguishable, and sundry capillary channels, previously invisible, become occupied by blood and show themselves. This first stage lasts for an hour, or in some cases perhaps two, and is followed by a phase of slowing of the blood-current. While previously a well-marked axial stream of corpuscles had been evident, with a peripheral zone of plasma devoid of corpuscles, the former now broadens out, the latter becomes less and less, and as it narrows increasing numbers of the clearer rounded hæmal leucocytes are to be seen in it travelling at a slower

rate than the more axial stream, and every now and then stopping beside the walls of the vessels, and after a short stoppage passing on again. The leucocytes conduct themselves as if they have become "sticky."[1]

As the current becomes yet slower all distinction between axial and peripheral streams is lost; the corpuscles, closely packed together, fill the whole lumen; the leucocytes in increasing number approach the vessel-walls; they adhere more firmly, and so long as a current is recognisable the action of the stream leads them to assume a pear-shaped appearance, the rounded ends pointing in the direction of the current.

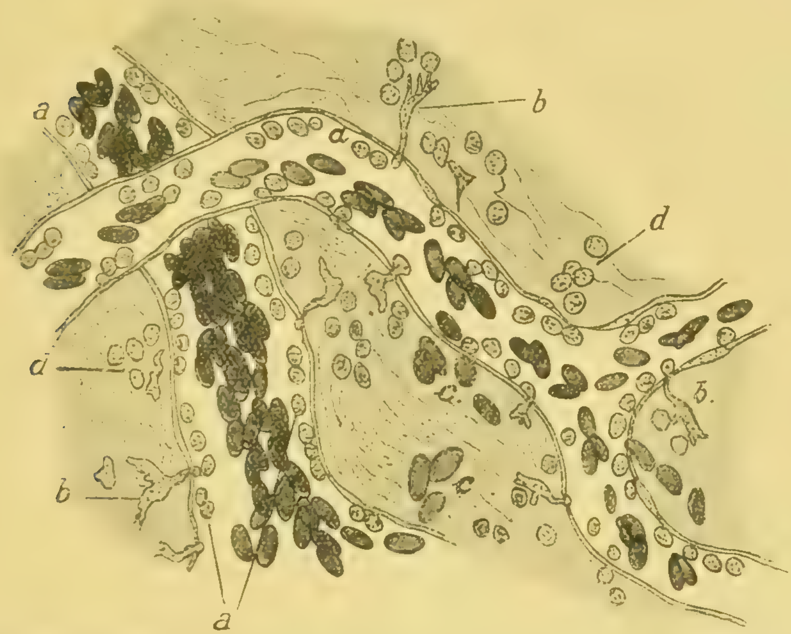

FIG. 67.—Inflamed mysentery of frog to show margination of leucocytes in the dilated capillaries (*a*); migration of leucocytes (*b*); escape of red corpuscles (*c*); accumulation of leucocytes outside the capillaries (*d*).—After RIBBERT.

As the stream slows gradually the corpuscles may at last move in a series of jerks synchronous with the beats of the heart; or frequently in the veins and capillaries the mass of blood may be seen moving slowly first in one direction, then in the other. Frequently one or other of these stages is followed by complete stagnation, or stasis, of the blood in the vessels of the injured area—I say frequently, for at other times little or no absolute arrest is seen in the vessels. Accompanying this stage, although observers employing other and chemical methods of inflicting

[1] Even so low down in the scale as Daphnia this same peculiarity is noticeable: there in health, as Mr. Hardy (18) has pointed out, the leucocytes move freely; but, if the slightest injury be inflicted upon the carapace, the leucocytes, previously unadhesive, soon show the tendency to adhere to the walls of the body-cavity beneath the region of injury and elsewhere.

injury have in general omitted to call attention to the fact, there is already a considerable oozing or exudation of clear fluid from the wound; there is, that is to say, an outpouring of lymph, and this apparently from the distended vessels. Now, with the slowing of the stream the leucocytes, accumulated next to the walls of the small veins and within the capillaries, pass from the interior to the exterior of these vessels; and, if the process be studied carefully with a higher power, it can be seen that this mode of passage is of an active, or apparently active nature.[1] A series of leucocytes can be distinguished, some of which are rounded or flattened, in immediate contact with the wall of the vein; others possess a prolongation passing into the wall; in others, again (or in the former if they be watched in the fresh specimen), the prolongation enlarges on the outer side of the small vessel while the portion of the leucocyte within the vessel becomes smaller. The final phase of this act of migration is that the whole leucocyte passes through, and is found in the lymph-spaces around the vessel-wall. This process of migration may be so general that in the course of five or six hours all the small veins of the region show a crowd of leucocytes situated along their outer surface. With these a greater or smaller number of red corpuscles may also make their escape.

In this modification of Cohnheim's experiment a further stage is to be recognised. While at first the fluid exuded was clear and relatively free from cells and cell-debris, now, as the inflammatory process continues, an increasing number of leucocytes is contained in the exudation. The leucocytes do not remain in the immediate neighbourhood of the vessels, but many of them pass on to the injured surface; still it would seem by active amœboid movement. Thus at the end of six hours this surface may be covered by a serum or fluid containing large numbers of these leucocytes. Here then we have the first step towards the formation of a scab or provisional protective covering to the wound.

Further observations cannot well be carried out in the pithed and curarised frog; but if an unpithed, non-curarised animal be taken, and the observations upon the earlier stage be neglected, it can be made out that if irritant matter do not find entry into the wound the process may be arrested at this point; the leucocytes upon the surface may break down, and with their breaking down and the formation of fibrin a soft scab be formed: the stasis of the blood in the distended vessels may be followed by a re-establishment of the current and slow return of the vessels to their former calibre, while beneath the thin, soft scab the epithelial cells rapidly proliferate. Within twenty-four hours there may be abundant evidence of this new growth of the epithelium tending to encroach upon and cover the wound. At the same time the region becomes less and less populated with leucocytes, so that—not to enter fully at this point into the reparative process—within

[1] The process can be fully made out if at this stage the wounded region be removed, fixed immediately in weak osmic acid, and prepared for examination by the higher powers of the microscope.

sixty hours the region may show little sign of the injury and consequent inflammation.

On the other hand, if irritants of a microbic nature enter the wound the process may extend, as an inflammation of the cornea. More especially if the water in which the frog is kept become foul, there is a tendency in the inflammatory processes to spread, and in the cells, both fixed and migrated, of the central area to break down, leading to the formation of a spreading ulcer. The steps of this sequence of affairs it is difficult to follow by continuous microscopic examination, partly on account of the increased opacity of the region, partly because the process extends over days rather than hours. Here, therefore, I merely mention this possible extension of the change with its main naked-eye appearances.

It is not possible by continuous observation to make out the steps of this more extensive inflammation characterised by excessive emigration of leucocytes and destruction of these together with the fixed cells of the tissue—the pyogenetic inflammation. Several observers, however, have followed its successive stages by means of examination of affected tissues at successive intervals after the infliction of injury.

Chapter 5.—The Experimental Production of Suppurative Inflammation

While, as shown by Councilman (26), Grawitz and de Barry (27), Steinhaus (28), Leber (29), and others, a suppurative inflammation may under certain conditions be brought about experimentally by the action of chemical irritants, such as mercury and turpentine; yet under ordinary pathogenetic conditions suppuration is induced by the growth of micro-organisms within the tissues. Hence it is better to study the conditions as induced by the inoculation of pus-producing microbes into one or other tissue. A very full series of observations upon the development of abscesses through the agency of the Staphylococcus pyogenes aureus has been made by Hohnfeldt (30). He inoculated small quantities of pure cultures of the microbe subcutaneously into rabbits. Four hours after inoculation the vessels of the region were found densely filled with corpuscles, and in them a commencing margination of the white corpuscles was discernible. Leucocytes were present within the tissue in numbers greater than normal; although, compared with later stages, they were infrequent. They were of two kinds—the mononuclear in the majority, the poly-morphonuclear in lesser numbers; both forms were congregated mainly around the line of entrance of the injecting needle. Many of the connective-tissue cells were so swollen as to be rounded rather than flattened. The injected cocci, lying in the lymph-spaces, were scattered through the tissue; in part free, in part already ingested by cells, not only by the leucocytes, but also by connective-tissue cells, the number within leucocytes being not inconsiderable. Preparations

made at the end of ten hours showed the same conditions, but more distinctly. There was ample evidence of migration of the leucocytes, margination in the congested vessels, various stages of passage through the vascular walls, and large collections of the cells in the perivascular lymph-spaces; from these they spread into the spaces between the bundles of connective-tissue fibrils. The cocci lay in the lymph-spaces in increased numbers, and the massing of leucocytes corresponded in position to the accumulation of microbes. In these regions the leucocytes were mainly polymorphonuclear, but in the boundary zone away from the cocci the mononuclear form predominated. At the end of twenty hours there was further accentuation of these conditions. As yet an abscess proper had not formed, but there were enormous numbers of leucocytes and also of micrococci; the fibrillæ of connective tissue were widely separated by the collections of leucocytes, which clustered round and hid the connective-tissue cells. With the completion of forty-eight hours a well-defined abscess had formed, separated sharply from the surrounding healthy tissue. The centre of the abscess was seen to consist of densely-packed leucocytes mingled with large growths of cocci. These leucocytes were almost entirely polymorphonuclear; and in this central area the nuclei of some showed fragmentation. Neither leucocytes nor connective-tissue cells showed the slightest indication of mitosis. In the central area all traces of the previous capillaries had disappeared; in the peripheral zone they were easily recognisable, being fully injected and showing a marginal disposition of their leucocytes, many of which could be seen (in osmic acid preparations) fixed in the process of migration. The majority of the cocci lay in these leucocytes. Even where the colonies of the microbes were thickest there the majority were intracellular. Passing towards the periphery the number of cocci became smaller and smaller. At the periphery they could be seen not only to be intracellular, but also free in the lymph-spaces; and Hohnfeldt, with other observers, saw them definitely grouped within the endothelial cells of the peripheral vessels. Thus it may be noted that at this stage the proliferating microbes extended into the healthy tissues outside the abscess. In the centre of the abscess the original tissue had wholly disappeared; nearer the periphery light streaks and bundles of the disintegrating fibrillæ could be recognised between the leucocytes. Not till about the tenth day did new growth of tissue begin to show itself. During the preceding six days there had been more breaking down of the polymorphonuclear cells, characterised by fragmentation of the nuclei and by fatty degeneration of the cell-substance. But by the tenth day the periphery had begun to assume the appearance of granulation tissue: it contained numerous capillaries and new-formed connective tissue with characteristic epithelioid cells or fibroblasts possessing large, oval, pale-staining nuclei. In these cells, as in the connective-tissue cells of the surrounding healthy tissue, the numerous steps of indirect cell-division could be made out. In this granulation tissue cocci were absent and leucocytes were infrequent. In the soft, cheesy, central area masses of

cocci were still present. Whether these were living or dead Hohnfeldt did not determine; he inferred (what has since been proved by several observers to be an unsafe inference) that inasmuch as they stained well with aniline dyes they were alive.

Thus, to sum up Hohnfeldt's observations, the processes occurring in a suppurative inflammation that ends in healing are the following:—

1. Primary multiplication of the pyogenetic organisms with no immediate reaction.

2. Congestion of the region of invasion, with margination of the leucocytes.

3. Collection, in the region, of mononuclear leucocytes; then immigration of polymorphonuclear leucocytes: multiplication of the cocci.

4. Ingestion of large numbers of the microbes by the polymorphonuclear leucocytes and other cells, including the endothelial cells of the vessel-walls.

5. Increasing immigration of leucocytes until the tissue becomes densely packed. This is accompanied by a yet greater proliferation of the microbes, which extend (*i.e.* are carried by lymph-streams or by cells) into the region outside the developing abscess.

6. Coincident destruction of the tissue of the affected part.

7. Degeneration of the leucocytes within what is now the sharply defined abscess.

8. Eventual proliferation of the connective tissue at the periphery of the abscess; formation of fibroblasts in the highly vascular surrounding zone; absorption, cicatrisation, and encapsulation of the debris of the leucocytes and micrococci.

There are not a few points in connexion with these observations of Hohnfeldt that deserve discussion; very possibly he has misinterpreted certain of the appearances. On the whole, however, he draws a full and accurate picture of the successive stages of suppurative inflammation, and I may defer discussion to a later review of the action of the leucocytes and of the formation of fibrous tissue respectively.

However, before leaving this general description of the series of anatomical changes induced by injury, there is another phase of the inflammatory process set up by pathogenetic micro-organisms which must not be passed over—I refer to those cases in which, instead of ending in repair, there is *extension and generalised disease.* The stages preceding extension vary with the nature of the microbe; thus, in some cases, the reaction to the invasion of the microbe is mainly leucocytic (as with inoculations of the micrococci of suppuration), in others it is mainly exudative or serous, the congestion of the vessels being followed by abundant exudation of serum into the tissues. This is the case in inoculation of animals—such as rabbits, guinea-pigs, and fowls—with cultures of micro-organisms which are peculiarly virulent in their behaviour towards these animals. Such a serous or exudative inflammation is, for instance, well seen if the vibrio Metchnikovi be inoculated into the pectoral muscles of a fowl. Within twelve hours, it may be,

the seat of inoculation becomes greatly swollen, and on section is found reddened and congested; while from it drains an abundance of relatively clear, faintly reddish serum containing but few leucocytes.

In such a case as this the micro-organisms appear to pass with ease from the centre of infection into the surrounding tissues, and thence into the lymphatics and general circulation, whence they may be obtained within twenty-four hours. Where there has been a well-marked abscess-formation in the region of invasion there, as already indicated, it is true that the microbes may be found outside the abscess at a fairly early period; but, in the main, proliferation is limited to the abscess, and the blood remains free and sterile. Under certain conditions of greater virulence of the pyogenetic microbes it is found that as the abscess extends it becomes ill-defined—there is no sharp demarcation between the collected leucocytes and the surrounding tissue; the columns of leucocytes spread indefinitely from the centre, and numerous micrococci are intermingled with them. Where this is the case there is a marked tendency for the microbes to find their way into the general circulation from this irregular peripheral extension along the lymphatic spaces, and to set up a condition of septicæmia as in the more serous inflammation described above.

Septicæmia, or the passage of micro-organisms into the blood,[1] with all the results of such a passage—the condition which sundry French observers have described as inflammation of the blood—is dealt with in another article. In septicæmia we pass beyond the local response to injury, we deal with a state of general systemic disturbance. Nevertheless certain phases of the septicæmic condition throw light upon the inflammatory process.

In the first place, it is of interest to note that when the infective micro-organisms and their products are within the vessels they fail to induce the cardinal symptoms of inflammation. They do not lead to exudation of fluid from the blood or to widespread diapedesis of leucocytes. The stimulus, whatever it be, which leads to these phenomena at the point of invasion is no longer called into activity when the noxa is within the circulatory apparatus. This is the reverse of what might be expected if the inflammatory process were primarily due to a modification of the endothelium of the vessel-walls by the irritant, a modification passively permitting the exudation and passage outwards of the leucocytes.

The statement that infective micro-organisms and their products circulating within the blood fail to induce inflammatory changes, would seem to need modification when the development of *metastatic abscesses* is taken into account—of secondary abscesses, that is, in tissues at a distance, and not in direct continuity with the original focus. But a study of the mode of production of these abscesses shows that the state-

[1] This is the sense in which the term *Septicæmia* is employed by pathologists and bacteriologists; by some surgical writers the word is employed as synonymous with *Toxæmia*; to avoid confusion there is now a tendency to utilise the more precise term *Bacteriæmia* to indicate the presence of microbes in the blood.

ment still holds. Such abscesses originate round emboli of pyogenetic micro-organisms in the capillaries. Sundry cocci are arrested in a capillary, proliferate, and fill the vessel. It must not be thought that the plugging or embolism is an immediate process in these cases—that the bacteria are present in the blood in such numbers that a cluster of them, passing into a capillary, blocks it. Experience shows that, with a bacteriæmia of this extent, death ensues so swiftly that there is no time for abscess-formation. Either the bacteria are contained in a small mass of infected blood-clot, which is the immediate cause of the blockage (as, for example, in abscess of the kidney secondary to infective endocarditis, and in lung abscesses following upon suppurative thrombosis of the lateral sinus), or, in other cases, isolated bacteria passing with the blood into a capillary are taken up by a phagocytic endothelial cell, and, instead of being destroyed, multiply, lead to the death of that and surrounding cells, and form a colony occluding the capillary. It is only when a minute vessel is thus occluded that the abscess-process begins, that is to say, when by this occlusion the vessel has become extravascular; and while it is true that, primarily, the arrest of pathogenetic microbes within the capillaries is often associated with a small accumulation of intravascular leucocytes and with degenerative changes in the vascular endothelium, the metastatic abscess, as such, forms not by accumulation of leucocytes in the occluded vessel, but around it; the leucocytes migrating from surrounding capillaries.

Chapter 6.—Inflammatory Fever

In the second place, through this study of advancing inflammation it is of interest to trace the very close relationship that exists between inflammation and fever. Besides the local changes here described, local injury is accompanied by systematic disturbances. These may be slight or grave. Take, for instance, progressive abscess-formation, or follow the development of a malignant carbuncle in man. At first the reaction is purely local, but very soon, long before any of the micro-organisms are capable of detection in the blood, there is a raised temperature and a slight febrile state, the fever becoming more and more evident as the local process becomes more and more extensive, until with the detection of the microbe in the blood the most severe fever, with constitutional disturbance, sets in. Local inflammation, then, without any other possible explanation than either the nervous irritation to which it may give rise, or the passage into the general circulation of the soluble products of bacterial growth and tissue-destruction, or both, may lead to the development of the febrile state. How large a share is played by these two possible factors it is difficult to say. That bacterial products injected into the circulation lead to the rapid production of the febrile state rests on ample evidence; but whether these act directly by inducing increased cellular activity, or indirectly by stimulating the cerebral centres, we cannot absolutely say. As yet we

have little accurate knowledge of the part played by the nervous system in the development of the febrile state. This, however, may safely be declared, that the more we study the continued fevers the more do we discover that these commence by a local inflammatory disturbance. The continued fevers of bacterial origin are the continuance, or rather the extension, of a primarily localised inflammatory lesion.

Chapter 7.—Summary of the Facts thus far brought forward

The main facts gathered thus far concerning the inflammatory process, and the conclusions to be drawn therefrom, may now be placed in order before I discuss in detail the various factors in the process. They are—

1. Injury, when it is not so widespread and severe as to lead to the death of the individual, is followed by a reaction on the part of the organism.

2. In unicellular organisms the continued vitality of the individual after injury, and in multicellular organisms the vitality of the individual cells, is dependent primarily upon the persistence of the nucleus; if this be destroyed or removed the rest of the cell is incapable of complete restitution and continued growth.

3. In unicellular organisms the reactive process is twofold, and consists of (*a*) destruction or removal of the irritant; destruction being brought about by a process of intracellular digestion, removal by extrusion of the irritant; (*b*) new growth of the organism.

4. This response to injury on the part of unicellular organisms is essentially reparative.

5. In multicellular organisms, with division of labour among the constituent cells of the individual, there is a separation of functions; the twofold local reaction to local injury is yet more clearly marked; but

(*a*) The destruction or removal of the irritant is *in the main* accomplished by the wandering cells of mesoblastic origin.

(*b*) The new growth to replace the tissue destroyed by the irritant proceeds *in the main* from the fixed cells of the tissue.

6. Ascending the scale of multicellular organisms, a division of labour and differentiation of function is discoverable among the wandering mesoblastic cells. Whereas in the lower forms of the Metazoa one form of leucocyte alone is present, in the higher forms two or more varieties can be distinguished which possess different properties and act differently towards irritants introduced into the system.

7. According to the nature of the irritant causing the injury, the leucocytes are actively attracted in greater or less numbers to the region of injury, surround the irritant, and remove or destroy it by means very similar to those employed by unicellular organisms. Where the irritant is present in the form of discrete particles, some at least of the leucocytes may incorporate the particles, and remove them or destroy them by a process of digestion. Others of the leucocytes in the higher Metazoa do

not act thus as phagocytes: nevertheless they are equally attracted to the focus of inflammation, and presumably tend to counteract the irritant by some other (extracellular) means.

8. While to the wandering cells appears to be allotted the main duty of removing deleterious and irritant matters, certain of the fixed cells of the organism, notably the endothelial cells of the vessels, also exert these functions.

9. Among the very large number of Metazoan forms in which no complete vascular system is present, this attraction of the leucocytes to the region of injury is at first the sole recognisable response to injury, proliferation of the fixed cells occurring in the neighbourhood of the injury at a later period. The relation between leucocytic migration and tissue-proliferation is, however, a variable quantity; there may be active proliferation in response to injury with little evidence of wandering in of leucocytes.

10. Among the higher Metazoa, in which there is a well-developed vascular system, the determination of leucocytes to the region of irritation still continues, and is in fact markedly aided by the participation of the vessels in the inflammatory process.

11. The vascular phenomena in inflammation may be regarded as serving two main purposes—(*a*) the pouring out of increased fluid into the injured area; (*b*) the afflux and diapedesis of leucocytes.

12. Even in the highest Metazoa, possessing fully developed vascular systems, the response to injury in a non-vascular area, such as the cornea, may be associated with no change in the surrounding vascular areas, but purely with a determination to the injured area of leucocytes already free in the surrounding tissues.

13. The second phase of the inflammatory process, that of tissue-repair, but very rarely occurs without evidence of previous migration of leucocytes and exudation from the congested vessels; nevertheless with certain mild grades of injury it can occur.

14. A comparative study leads inevitably to the conclusion that the determination of leucocytes to the region of injury is the most constant and most characteristic early response to injury recognisable throughout the Metazoa, and that it must be regarded as the most important factor in the first stage of the inflammatory process. The vascular phenomena noticeable in the higher Metazoa must be regarded as a second and highly important adjuvant factor of later development. New tissue-formation is the prominent characteristic of the later stages of the process.

15. As among the Protozoa, so in the Metazoa, the response to injury is consistently in the direction of repair of injury.

This general survey of the response to injury throughout the animal kingdom demonstrates most clearly that the same broad principles, the same methods of defence and repair on the part of the organism, are called into activity from the lowliest forms to the highest; that, in fact, no line can be drawn to separate one set of phenomena as truly

inflammatory from another set which, while also a response to injury, is non-inflammatory. Although it is true that the term inflammation implies a reddening and congestion of the vessels, we find upon closer examination that reddening and congestion are not the fundamental but superadded features in the process of repair of injury—features superadded as the organism advances in its place in the animal kingdom. Thus if we are to comprehend the process satisfactorily, we must pass beyond the narrower acceptation of the term.

Having thus sketched broadly the general phenomena of the inflammatory process, it will be well now to describe in fuller detail the factors of this process among the higher vertebrata, and to bring together the more important results of the study of the respective functions of the wandering cells, the vessels, the fixed cells, and the nervous system in inflammation.

PART II.—The Factors in the Inflammatory Process

I.—The Part played by the Leucocytes

The Leucocytosis of Inflammation.—As I have already shown, there is more than one form of leucocyte in the mammalian organism, and these several forms would seem to possess different attributes acting differently in response to local injury. Though I may safely leave the reader to gain a knowledge of the features of the original white blood-corpuscles from the article upon the Blood in this volume or from other modern works devoted wholly to a consideration of the blood (31, 32, 33), it is still necessary to call attention to the other wandering corpuscles present in the area of inflammation but not derived from the blood. We must, in short, make the following provisional classification of the leucocytes concerned:—

Haematogenous
- Polymorphonuclear (neutrophil and amphophil, "polynuclear").
- Eosinophil (coarsely granular, oxyphil).
- Mast-cell[1] (coarsely granular, basophil).
- Lymphocyte.

Chapter 8.—Histogenous Leucocytes

The part played by these is most clearly seen in the study of inflammation of the peritoneum. Many years ago Cornil and Ranvier (34) called attention to the very active proliferation of the endothelial cells of the great omentum in inflammations set up by the injection of dilute solutions of silver nitrate. They pointed out that these cells, flat and lamellar under ordinary conditions, become

[1] The mast-cells are here included in accordance with the general scheme of writers upon this subject. Personally I am a little doubtful as to whether this is their right position, *i.e.* whether the mast-cells seen in inflammatory foci have wandered as such from the blood.

greatly enlarged with swollen nuclei which, within a few hours, undergo direct division, so that many cells come to possess two or three nuclei. Indirect division (mitosis) is only seen, according to Cornil and Toupet, in forty-eight hours. Some more recent observers have recognised it much earlier, Dr. Beattie (35) as early as the tenth hour. So swollen are the cells that they project prominently from the surface, being often pear-shaped and attached merely by a pedicle. As a result of the active proliferation, here and there large, semi-detached clumps of these cells may be made out. These authors did not study the exudate; this has been done by more recent observers, notably by Drs. Durham (36) and Beattie. The former, employing non-lethal intraperitoneal injections of several microbes, has described the same changes in the omentum as those described by Cornil and Ranvier, and has noted, more particularly, that these swollen cells give origin, by direct division, to large, clear, mononuclear cells or leucocytes. These may be derived from the peritoneum generally, but the omentum is especially active in this respect. He identifies these cells with Metchnikoff's "macrophages," and Dr. Beattie has made a full study of the same. They are, according to him, the most characteristic form of leucocyte seen in peritoneal inflammation. After non-fatal peritoneal injection of the B. coli in the guinea-pig, he first observed an increase in the polymorphonuclear cells of the peritoneal fluid, which begins three hours after the injection and reaches its maximum in from six to thirty hours. Mononuclear leucocytes are first seen to increase in number about the eighth hour. On an average these are in numbers equal to or even greater than are the polymorphonuclears. From now onwards (in non-fatal as distinguished from fatal cases) they definitely preponderate. As during the next two days resolution proceeds, the polymorphonuclears become fewer and fewer until the few cells present in the exudate are almost entirely mononuclear. These mononuclear cells (the hyaline cells of the late Prof. Kanthack and Mr. Hardy (37), and of other observers) vary in size. According to Dr. Beattie there is every transition from small cells resembling lymphocytes with a round or kidney-shaped nucleus rich in chromatin, and with scanty protoplasm, up to cells four or five times as large, having a rounded or kidney-shaped nucleus which does not stain nearly as deeply as that of the smaller forms, but shows deeply-staining nodes of chromatin in the nuclear network. These larger cells have abundant cytoplasm, often showing extensive, fine vacuolation. In these respects the cells are identical with the swollen endothelial cells of the omentum. Nor are they merely passive agents—cells cast off in a moribund condition from the inflamed peritoneum and undergoing degeneration. They are phagocytic; they take up bacteria, though, in this respect, they are not, with certain exceptions, so active as are the polymorphonuclears. Thus, if tubercle bacilli be injected, they are found, in a few hours, almost exclusively within the mononuclear cells and not in the polymorphonuclears. This is in harmony with our general experience that polymorphonuclear leucocytes, while not negatively chemiotactic to tubercle

bacilli, are not potently attracted thereto, so that these more leisurely mononuclears have the opportunity to take them up. What is most characteristic is that these mononuclear cells are active cellular phagocytes; they take up other cells of the exudate—polymorphonuclears, eosinophils, and red blood-corpuscles. A single large mononuclear cell of a peritonitic exudate may often be seen containing three or four other cells or the remains of the same.

There can, therefore, be no doubt that, in peritoneal inflammation at least, an important series of free cells or leucocytes[1] is of endothelial or tissue origin; the question is whether all these mononuclear cells are of like development. While clearly the larger forms are indistinguishable from the swollen cells of the peritoneal endothelium, and while the time of their appearance in the exudate coincides closely with the onset of active proliferation of that endothelium, we have the apparently contradictory statement that every transition is also to be observed between them and small lymphocytes; while other observers studying lymphocytes proper are equally convinced that these cells never develop into the large hyaline cells above described. Now lymphocytes proper may be found in the peritoneal exudate. These apparently contradictory results may be harmonised by pointing out that, in the first place, in the very earliest stages, most cells are indistinguishable, and that, in the second place, a distinction can frequently be made out between the lymphocyte proper and the embryonic cell of endothelial origin. The former has a deeply-staining, rounded nucleus; the latter a nucleus which, while also deeply staining, tends to be indented. There is, however, another difficulty; if the omentum be examined during the period of peritoneal inflammation, its vessels are seen to contain mononuclear cells which, like these "hyaline" cells of the exudate, are devoid or almost devoid of granulation, and these intravascular cells are not to be distinguished from the medium-sized hyaline cells of the exudate. Why cannot some of the mononuclear cells of the exudate be hæmatogenous? There is, apparently, no reason why we should deny this hæmatogenous origin of some at least of these cells, nor would it seem that, making this admission, we land ourselves in further difficulties. On the contrary, the evidence accumulating of late years appears to point in one direction, namely, that the mononuclear cells seen within the vessels during the process of inflammation are similarly of endothelial origin. Metchnikoff, from 1883 onwards, was the first to suggest that the large mononuclear leucocytes seen in vessels and lymph-glands are identical in their properties and characters with the endothelial cells of these tissues, and

[1] It may be questioned whether it is right to speak of wandering cells, of tissue origin and not necessarily of vascular origin, as leucocytes, that term having first been employed as synonymous with white blood-corpuscles. But, on the assumption that has obtained until recently—that practically all the wandering cells seen in inflammation are derived from the blood—it has been customary to speak of all orders of these cells as leucocytes, and, certainly, all have the more general characters, rendering it difficult to distinguish them one from the other save with care. Thus, as a matter of custom and of practical utility, I continue to speak of all these various cells indifferently as leucocytes.

he directed attention to their peculiar properties of ingesting the leucocytes, and named them "Macrophages" (a barbarous but a convenient term). Dr. Ruffer's (38) studies of the lymph-glands wholly confirmed these observations. The fullest studies upon the histology of these cells are by Mallory (39), who described, with great detail, the large cells with slightly-staining, grooved, or indented nucleus, present more particularly in the lymph-glands in typhoid fever, and possessing, in short, all the characters of Metchnikoff's macrophages. He describes them as originating from the proliferation of the endothelial cells of lymph-spaces, lymphatics, vessels, and, in fact, all endothelial structures. He has observed their mitosis, and has demonstrated the migration of such proliferated endothelial cells into the adjoining connective tissue (Fig. 68). These observations were confirmed by Councilman, in his studies upon keratitis (24). We have, indeed, to recognise the very active part played by the vascular endothelium in inflammation, its pronounced proliferative and phagocytic properties. As pointed out by Abbott, Nicholson, and myself (40), within ten minutes after inoculating the B. coli into the circulation, the endothelial cells of the liver capillaries are swollen and have taken up numerous bacilli (Fig. 69). Before our observations, Werigo (41) had demonstrated the process whereby hepatic endothelial cells give off pseudopodia, by which anthrax bacilli are seized and subsequently englobed. Recently Behring and Much (42) have called attention to the great phagocytic powers of the endocardial endothelium. As Dr. Beattie points out, in omental inflammation the cells lining the veins become swollen and then detached from the wall, and various stages of the separation can be made out. Study of the sinuses of the spleen in typhoid (Mallory) shows the process very well; the lining cells swell to three or four times their original size and become separated, so that a sinus may become distended with these free cells. As they swell, their cytoplasm becomes vacuolated, and polymorphonuclears and other cells are seen to be ingested. Without entering into a discussion of the finer details of nuclear staining (*vide* Dr. Beattie's article) I would point out that the evidence now accumulating tends to the conclusion that Ehrlich's mononucleated non-granular blood-cells (43)

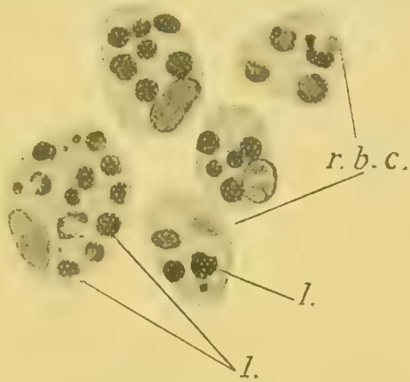

FIG. 68.—Large cells of endothelial origin (macrophages of Metchnikoff) from centre of lymph-gland (*l*) in typhoid fever which have actively taken up lymphocytes and red blood-corpuscles (*r b c*). MALLORY.

FIG. 69.—Endothelial cell of capillary of rabbit's liver, fifteen minutes after in- [illegible] inoculation of culture of B. coli, showing bacilli ingested and undergoing disintegration. (The whole of the nucleus is not here in focus.)

are of endothelial origin.[1] Contrary to Gulland (44), Saxer (45), and Uskow (46), therefore, I am of opinion that there is far from being a common origin for all the white blood-corpuscles; one group at least is of endothelial origin. And thus, recognising that these are capable of migration, it must be admitted that cells of this order seen in exudates may be of both local and hæmatogenous source.

A word may here be said regarding the fate of these large mononuclear cells. Evidence seems to show that they do not, to any large extent, wander back into the blood-vessels. Various stages of degeneration of these cells may be recognised in the later stages of peritoneal inflammation; they tend to be extensively vacuolated, and thus the conclusion is that they in the main eventually disintegrate locally. While this appears to be true in connexion with bacterial inflammations, where more inert substances are taken up they clearly are capable of wandering in considerable numbers back into the circulation. Thus Metchnikoff points out that, if washed nucleated red corpuscles of the frog be injected into the peritoneum of a warm-blooded animal, large mononuclear cells containing the easily recognisable remains of the corpuscles can be detected after several days in the mesenteric glands, the vessels of the liver, and the spleen. Cells of the same order, which have not become free, evidently, according to Ranvier, take an active part in the formation of peritoneal adhesions. Muscatello (47), Graser (48), and Borst (49), unite in the opinion that the endothelium of serous surfaces can form connective tissue, though of late von Brunn (50) and Mönckeberg (51) have strongly contested this view, at least as regards serous endothelial cells. Their objections are not, to me, wholly convincing. More recently Baumgarten (52) has brought forward what appears to be definite evidence that vascular endothelium under mild grades of irritation gives rise to fibroblasts and connective tissue.

Epithelial Leucocytes.—Mononuclear cells of endothelial origin seen in inflammation of solid tissues, noticeably in tubercle formation, are, from their general appearance, often spoken of as epithelioid cells. But if we employ the term epithelium, as is usual in English-speaking countries, to denote membranes derived from the primitive epiblast or hypoblast, this usage is apt to cause confusion. There are, however, true epithelioid cells; I refer to the large phagocytic cells seen in pneumonic conditions, clearly derived from the flattened epithelium lining the air-sacs. With Pratt (53) we must recognise, in the pneumonic exudate, two forms of large mononuclear cells: (1) large cells, round or oval, with a crescentic, vesicular nucleus placed towards the periphery and apt to contain cell-inclusions, and (2) a cell present in the early stages of acute lobular pneumonia, larger than the polymorphonuclears, but not so large as the form just mentioned, but, like that, having a large, vesicular, indented nucleus and a very slightly granular protoplasm. These also are

[1] With these I do not include the neutrophilic and other myelocytes seen in the blood in certain disorders: they, it need scarcely be said, are cells of a different order, clearly derived from the bone-marrow.

phagocytic, and Pratt expresses himself as doubtful regarding their origin. From his description, and since they are also found in the capillaries and in the tissues, it would seem clear that these are the endothelial mononuclear leucocytes mentioned above.

Plasma-Cells.—There is another form of mononuclear cell which must, we think, be included in this series, although, as to its properties and origin, there has been and still exists a very active controversy. This is the almost notorious plasma-cell. Unna (54) first named these in 1891, or rather misnamed them, using a term previously employed by Waldeyer for another form of cell. Unfortunately his description was not wholly adequate, and various later observers have evidently included and described under this term cells of more than one order, so that confusion is worse confounded. The cell which most closely conforms to Unna's description, and which, therefore, I regard as the plasma-cell proper, has the following attributes :—it has a relatively small, round or oval, not indented nucleus, coarsely granular, rich in chromatin and, further, staining darkly ; this nucleus is situated excentrically. The cell-body stains deeply with Unna's methylene blue ; the shape within the tissues is liable to considerable variation—often rounded or oval ;—the cells may be polygonal or even drawn out into a spindle ; they are obscurely amœboid. As to the possession of phagocytic properties, opinion is somewhat divided. The general agreement is that they are not seen to take up bacteria ; they may, however, contain inert particles of foreign matter such as vermilion or coal-pigment. As they grow larger and older, the cytoplasm tends to become somewhat vacuolated, and the nucleus to be less deeply stained. As to their eventual fate, nothing definite can yet be said at present. Cells having these characters are normally present in lymph-glands, spleen, and bone-marrow, and here every transition can be made out between them and the ordinary lymphocyte, which similarly, it may be noted, has a small, round, deeply-staining nucleus (even more deeply staining so as to appear homogeneous). According to von Marschalko (55), they may be noted in any inflammation within twenty-four hours. More recent observers state that they do not appear in quantity within the zone of inflammation until several days have elapsed. Now, as noted by Justi (56) and Councilman (24), there is normally around the veins a lymphoid sheath, and in inflammatory conditions this sheath becomes noticeably augmented. The cells here multiply by direct division, and, in addition, here and there mitoses are visible (Justi). That lymphocytes are endowed with faint amœboid activity (Wlassow and Sepp (57), A. Wolff (58)), and that, further, they migrate from the vessels, has now been pointed out by several observers (Councilman, Almkvist (59)). It is quite possible, therefore, that the increase in the perivascular lymphoid sheath is in part due to migration from the vessels, and, therefore, that some at least of the hæmatogenous lymphocytes develop into plasma-cells. Though, admitting this, it seems to me evident that the majority of the plasma-cells are derived from the proliferating perivascular tissue, and thus are not immediately hæmatogenous. It is on these grounds that I

am led to include them here among the histogenous inflammatory leucocytes, in order to emphasise the fact that not all the leucocytes seen in the field of inflammation are of vascular origin.

I have, I admit, here collated and selected out of a large number of very divergent descriptions those statements regarding the plasma-cell which conform with the conclusions I, personally, have reached regarding them. I am fully prepared to find that not all who have studied these cells will agree with what is here laid down, but to discuss the divergent views would occupy too much space. The reader, however, will find references

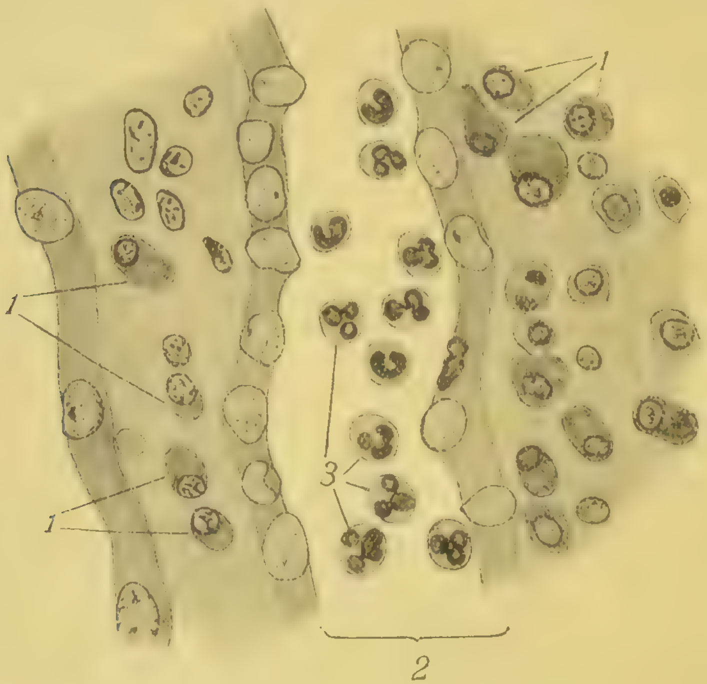

FIG. 70.—From a case of acute interstitial nephritis (man), drawn by camera lucida, $\frac{1}{12}$ Zeiss, ocular 2. Showing plasma-cells (1) in the interstitial tissue between the tubules. The epithelium of the middle tubule (2) is degenerated; the tubule contains polymorphonuclear leucocytes (3). [After COUNCILMAN.]

to the leading papers bearing upon these cells given in the bibliography at the end of this article. The views here given in the main agree with those of von Marschalko, Paltauf (60), Justi, Mallory, and Councilman. In their properties the cells here indicated conform largely to Maximow's "polyblasts" (61), cells which Maximow regards as distinct from the plasma-cell.[1]

Free Cells—Leucocytes—derived from other Tissues.—In the

[1] Important as is Maximow's work, and obvious as is the amount of study given by him to the subject, I cannot but feel that in the tissues selected by him and by the methods employed he has failed to distinguish between young lymphocytes and cells of endothelial origin, and that, had he studied the peritoneum, for example, he would have reached other conclusions.

experimental inflammations of the cornea it can be recognised that the tissue-cells of the boundary zone in which there is no actual destruction undergo active proliferation. The corneal corpuscles, for example, as already indicated, become swollen, send out processes towards the point of injury, their nuclei stain more deeply, undergo division, and now two young cells of embryonic type are present where one had been before. These young cells are of the hyaline or mononuclear type and, what is more, like the cells of endothelial origin, actively take up polymorphonuclear and other cells. Nor are the connective-tissue corpuscles alone in giving rise to cells of this order. Highly complex tissue-cells, like muscle fibres, when injured, are apt to exhibit direct division and multiplication of their nuclei; these nuclei are apt to separate from the main mass, carrying with them a small body of surrounding cytoplasm. This process in connexion with the degenerating tadpole's tail has been well described by Metchnikoff (62), Barfurth (63), Griffiths (64), and others. When so separated, these cells are not to be distinguished from hyaline mononuclear leucocytes and, like them, actively digest cell-debris, and so forth.

Clasmatocytes.—In certain fine connective-tissue membranes, both in warm- and cold-blooded animals, there are to be seen considerable numbers of large, apparently wandering cells, elongated or much branched, with a rounded or elongated nucleus which Ranvier (65), on account of their tendency to cut off or leave behind them in their wanderings small remnants of protoplasm, has termed clasmatocytes. Marchand (66) has included them among his leucocytoid cells. According to Ranvier, these originate as leucocytes—*i.e.* are derived from the blood—which have become more or less stationary in the tissues, and, on one hand, in their proliferation may give rise to cells of the exudate, and on the other hand, may develop into true connective-tissue cells. While agreeing with Ranvier in this latter respect, Marchand denies that they originate from ordinary leucocytes, and regards them as identical with what Saxer (64) has termed "primitive wandering cells," which can give rise to leucocytes and nucleated red corpuscles. He thinks that by repeated division they develop lymphocytes, and that they gain entrance into the circulation as a form of mononuclear leucocyte, and, as already stated, that they may take part in the formation of connective tissue. Maximow concurs in holding that they may form fibroblasts and mononuclear "polyblasts." But now, as Lubarsch (67) points out, an identical form of cell is to be found in keratitis, with the same remarkable long processes, which are apt to be cut off and lie isolated in the tissues. If we then can determine the nature of these cells, we may arrive at some conclusion between these divergent views, but here, I must confess, there are difficulties. Lubarsch regards the characteristic corneal cells with spear-like processes as derived from mononuclear leucocytes which wander into the part. Grawitz (68), on the other hand, holds that these cells are modified corneal tissue-corpuscles. Councilman, and before him Senftleben, are very clear in their descriptions of the way in which, in certain grades of

keratitis, the peripheral zone of corneal corpuscles enlarge, send out processes into the necrosed area, and proliferate. This process we have just described. Their statements, thus, are in agreement with that of Grawitz.

It will be seen, reading over the description of these various forms of cells which we regard as histogenous, as distinguished from hæmatogenous, that certain features are common to all of them: the tendency to attain to large size; the amœboid character; the rounded, or, at most, kidney-shaped nucleus; the tendency to take up other cells; the liability, on the one hand, in proliferation, to give off wandering cells of the mononuclear type, on the other hand, to develop into fixed tissue-cells. Taking all these facts together, it will be seen that the clasmatocytes group themselves with the histogenous group of wandering cells, and as such I must classify them. In short, much, if not all, of the contro-

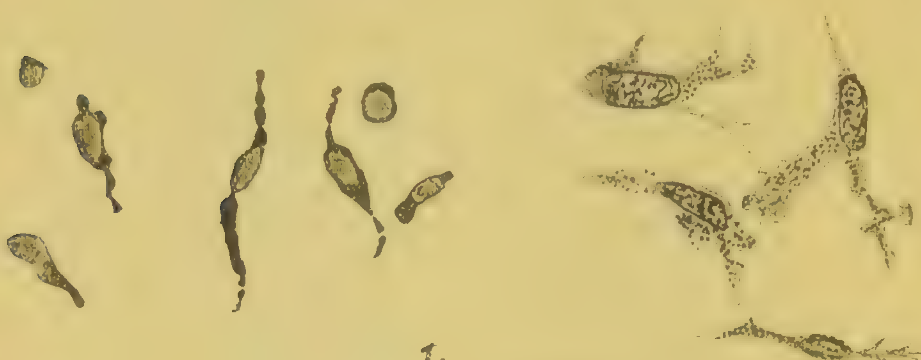

FIG. 71.—Clasmatocytes. After (1) *Ranvier* and (2) *Maximow*.

versy regarding these different forms of cells becomes assuaged if we regard the cells of the mononuclear type with relatively abundant protoplasm—the so-called hyaline cells—as of endothelial and tissue origin, whether they occur within the blood or in the inflammatory focus.

To those who have not followed the copious literature of the last few years, these questions regarding the nature of the different forms of cells seen in inflammation may appear to be small and unimportant, and the controversy regarding them to be very petty. But much depends upon the proper solution of this question, more particularly as regards the nature of the new-formed tissue which develops in areas of inflammation, and the difficulty in arriving at correct conclusions is very great. Anyone who has studied inflammatory tissues will find out that, at first, classification of the different forms of cells seen seems to be almost hopeless. As a matter of fact, the youngest forms of newly developed cells are often so exactly alike that no means at present at our disposal serves to distinguish them; hence, for example, the controversy whether the large mononuclear cells give origin to lymphocytes. It is only by carefully following the successive stages seen in the proliferation of any one form

of cell that we can arrive at any conclusion, and by a combination of methods, for the employment of only one or two methods of staining is apt to mislead.

Let me once more repeat that I am fully prepared to find that others do not agree with the conclusions here reached; nay, more, I would add that I am personally fully prepared to modify my views regarding these cells in the light of further research. In the meantime, to sum up, let me say that the completed table of the leucocytes concerned in inflammation would appear to be the following:—

Hæmatogenous.	POLYMORPHONUCLEAR (polynuclear, finely granular oxyphil, neutrophil, and amphophil cell). EOSINOPHIL (coarsely granular oxyphil, macroxycyte). MAST-CELL (coarsely granular basophil).	Originating in mammals from the bone-marrow, and migrating from the blood into the inflammatory area.
Histo-hæmatogenous.	LYMPHOCYTE. PLASMA-CELL. ENDOTHELIOID LEUCOCYTE (mononuclear leucocyte, hyaline cell (in part), "epithelioid cell" (in part)).	Originating from lymphoid tissue and from vascular and other endothelia respectively; present in inflamed area *either* by migration from blood *or* as result of local proliferation.
Histogenous.	EPITHELIAL wandering cell (large hyaline cell, in part). CONNECTIVE TISSUE wandering cell (including CLASMATOCYTE). MUSCLE AND OTHER tissue wandering cells.	Originating locally as result of local tissue proliferation.

CHAPTER 9.—SUMMARY OF PROPERTIES OF DIFFERENT FORMS OF LEUCOCYTES

And here, though in so doing I to some extent anticipate and refer to matters to be discussed in some detail later, it is most convenient to sum up briefly the facts determined regarding the parts played by these various forms in inflammation.

Polymorphonuclear Leucocyte.—In acute inflammation, when the irritant is not too intense, this is the form most often attracted to the focus of irritation, migrating most rapidly and in the greatest numbers. It is the characteristic pus cell; is actively phagocytic, particularly for bacteria; secretes bodies of the nature of enzymes and, either while active or in the process of dissolution, liberates antitoxic and antibacterial substances. It may—(1) wander back into the lymphatics or blood-vessels; (2) undergo dissolution and disintegration *in situ*; or (3) be ingested by the proliferating tissue-cells and mononuclear leucocytes. It has nothing to do with tissue formation (69).

Eosinophil Leucocyte.—This is also actively attracted, and that at an early period, towards the inflammatory focus, migrating from the surrounding tissues and also from the vessels, but it is never the preponderating cell present. In

peritoneal inflammations it is found in great numbers in the omental vessels, and in sub-acute and chronic inflammations of certain tissues, such as the skin, may also be relatively abundant. Very rarely is it seen to ingest bacteria, so that, to all intents and purposes, it is non-phagocytic. Kanthack and Hardy (37) and Hardy and Wesbrook (70) have ascribed a secretory activity to these cells, associated with the reduction in number and apparent discharge of the coarse granules, but later observers have failed to confirm their observations. The mode of action, therefore, of these cells remains unsettled. Opie has noted (71), that during the course of various pyogenetic infections, this form of cell disappears wholly or in part from the peripheral circulation, and after injection of a variety of bacteria into the peritoneal cavity of guinea-pigs he noted a similar disappearance; but now, examining the mesentery, during the height of the infection, the eosinophils were found collected in the blood-vessels, actively migrating into the peritoneal cavity, where they were collected in considerable numbers upon the surface of the omentum. They clearly, therefore, have a part in the inflammatory process, but what that part is must still be considered undecided; while there are indications that they proliferate *in situ*, all observers agree that they take no part in the formation of new tissue.

Mast-cell.—This is seen particularly in sub-acute inflammations (the coarse basophil granules, staining intensely with carbol-thionin and basic aniline dyes, and taking on a metachromatic nuance, must not be mistaken for clusters of small cocci). The nucleus stains feebly, according to the usual descriptions. Professor Miller of the University of Missouri has shown me his preparations, and permits me to refer to them. They definitely show that what has been taken for a feebly staining nucleus is a court or area where once the nucleus had been. The actual nucleus undergoes disintegration and discharge. This cell is sluggishly amœboid, and may detach portions of its cytoplasmic processes with their contained granules along the track taken by its pseudopodia. Nothing has been made out regarding the activities of this form of cell, save that Maximow (61 *b*) shows that in the course of the inflammatory process it undergoes atrophy and disintegration (72). Professor Miller's studies confirm these views, and indicate further a complete want of relationship between the relative abundance of hæmal and tissue mast-cells in inflammatory states.

Lymphocyte.—This is only slightly amœboid, and does not migrate very actively from the vessels to the injured area in acute inflammations. It is, however, capable of this migration, and, in some chronic inflammations, is the preponderating cell ("small round cell"). It is found more particularly in masses around the vessels, and this as a result of—(1) migration; (2) proliferation of the pre-existing lymphoid tissue. It is not phagocytic for bacteria, but may ingest particles of inert matter. The small lymphocyte, with a scarcely noticeable zone of cytoplasm, may give origin to the middle-sized lymphocyte, with more cytoplasm and deeper staining round or oval nucleus, and to the *plasma-cell* (73). There is no evidence that these plasma-cells are actively wandering, or that they return to the blood; they occur especially in connexion with the formative and chronic inflammations, but whether they actively participate in the formation of new fibrous tissue is still a matter of debate.

Histogenous Wandering Cells.—These appear in the inflammatory area in general at a definitely later period than do the polymorphonuclears and the eosinophils, and in certain forms of inflammation (*e.g.* of serous membranes) may become the preponderating type, exhibiting well-marked phagocytic

properties, being not so active as regards most species of bacteria as are the polymorphonuclear leucocytes, but peculiarly active as regards other cells and cell-debris. They are sluggishly motile, and though those of vascular endothelial origin may migrate from the vessels into the tissues, they are rarely recognised passing back into the vascular system from the inflammatory area; they are apt to become vacuolated. They multiply both by direct division and mitosis. They may—(1) undergo local necrosis and disintegration; (2) may form giant-cells, either by plasmodial fusion or by direct division of the nuclei; or (3) may be active factors in the formation of new tissue. Certain forms (*e.g.* those derived from corneal corpuscles, and the clasmatocytes) give off frequently long pseudopodial processes.

A word should here be said concerning sundry cells of later development, appearing as a result of inflammation—giant-cells, Ranvier's cells, and Gluge's corpuscles. Of these the last are evidently leucocytes of the hyaline type which have taken up the fatty products of tissue-degeneration; the second—colossal cells breaking down with great ease—are of endothelial origin. Giant-cells would seem to be of more than one variety; some appear to be due to aberrant cell-growth, wherein the nuclei undergo division without the protoplasm of the cell-body following suit. The characteristic giant-cells of tuberculosis and chronic inflammation may now be said with fair certainty to be plasmodia, in all respects comparable to the masses of fused cells seen to form in the lower animals around foreign bodies, and by Kanthack and Hardy around masses of bacteria in the lymph of frogs outside the body. The observations of Borrel (74), Duenschmann (75), and Faber (76) strongly support this opinion.

Chapter 10.—Phagocytosis

In the case of most pathogenetic micro-organisms, after inoculation into the organism, a very considerable proportion are to be discovered, sooner or later, within wandering cells which have collected in the region of inoculation. I have already mentioned more than one case of this nature in discussing the comparative pathology of inflammation. Evidently under certain conditions one of the functions of certain of the leucocytes is to attack and incorporate bacteria. The leucocytes having these properties in mammals are more especially the polymorphonuclear and the non-granular or faintly granular mononuclear cells of endothelial and tissue origin; the former, as already indicated, migrating from the blood, coming more rapidly into action and being most active from a very early period in tissues abundantly vascularised; the latter, in the main of local development, becoming active at a later period, and then acting as phagocytes towards other cells as well as bacteria. It is, for instance, the polymorphonuclear cell which is found in overwhelming numbers in an extending subcutaneous abscess, and these are seen to contain great numbers of the micrococci.

The conditions leading to this phagocytosis have been worked out in

remarkable detail by Metchnikoff. He has amply demonstrated that the microbes can be taken up in a living condition. Thus, if the Vibrio Metchnikovi (a form closely allied to the cholera spirillum) be inoculated into the anterior chamber of the eye of an immunised animal, within a very few hours phagocytes are seen filled with the small, slightly curved vibrios. If now one such cell be isolated, placed in a drop of broth upon a cover-slip, made into a hanging-drop preparation and examined under the microscope, it is seen that the broth causes the death of the leucocyte; while with time, and favourable temperature, the microbes proliferate rapidly and completely fill the corpuscle until it disintegrates, whereupon they proceed to multiply in the surrounding fluid. This seizing and incorporation of microbes does not then necessarily lead to their death. In certain cases of acute disease there may be

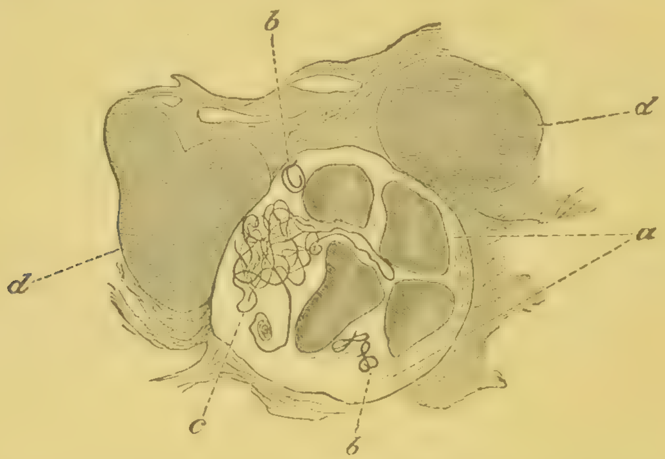

FIG. 72.—Resolution of acute infectious disease (relapsing fever) spleen pulp of monkey (a Macacus), showing (*a*) microphage, multinuclear, with incepted spirochætes; (*b*) solitary, and (*c*) forming dense tangle, (*d d*) nuclei of splenic tissue (Zeiss, $\frac{1}{18}$, ocular 4; × 1515 diam.). [METCHNIKOFF.]

abundant phagocytosis, and the disease progress nevertheless; the phagocytes being destroyed by the products of the incorporated organisms. This is the case in mouse septicæmia, in swine erysipelas, and (as has been shown by Gabritchewsky (80)) in diphtheria. As Roux remarks: "Ils ont fait de leur mieux en englobant les microbes, mais ceux-ci se sont adaptés au milieu intérieur des cellules, et ils ont triomphés" (77).

In other less acute diseases, such as gonorrhœa, and in chronic maladies, such as in tuberculosis, leprosy, and glanders, the bacilli may in certain stages be found within the cells and rarely free in the lymph-spaces, they appear to be almost parasitic, after the manner of the microsphæra previously referred to as infesting the amœba. In these cases it would seem as though the toxic properties of the microbes and the antagonising powers of the cells were nearly balanced. In tuberculosis, for instance, it is not unusual to find in the giant-cells some bacilli which

evidently are undergoing degenerative changes, staining poorly and irregularly, or but faintly traceable as unstained, translucent shadows, while elsewhere they are apparently proliferating despite their intracellular position.[1]

And this equality, or almost equality of the resisting powers of cells and microbes may explain the chronic nature of the diseases above

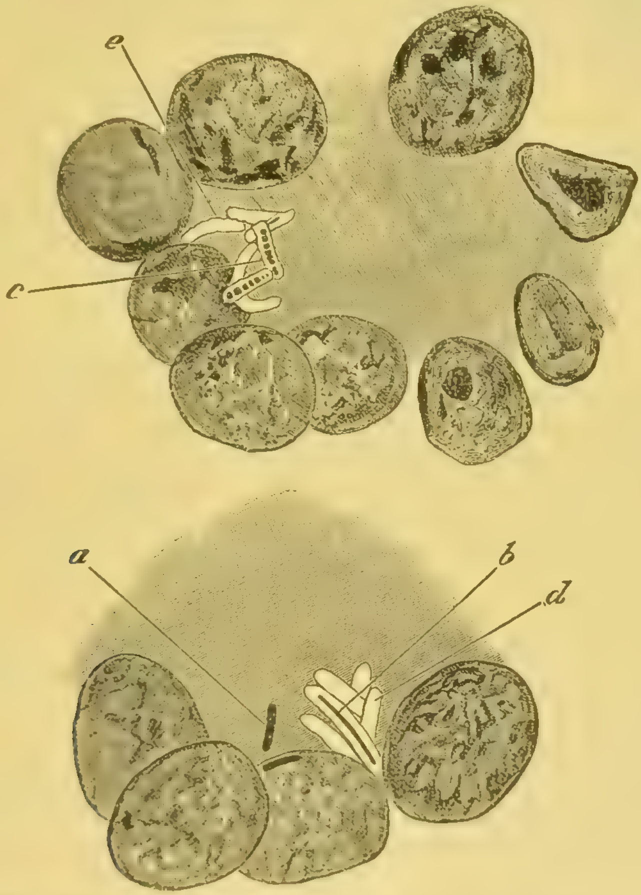

FIG. 73.—Two giant-cells, seen under high magnification (×1515 diam.), from a rodent, the spermophile, [illegible] with tuberculosis, to show stages in the destruction of the bacilli. *a*, unaltered bacillus; *b*, bacillus staining badly, and with greatly thickened capsule; *c*, bacillus granular and breaking up; *d e*, "shadows." [METCHNIKOFF.]

mentioned. Nevertheless, in general, it may be stated that there is some relationship to be recognised between the amount of phagocytosis and the virulence of the microbe; the more virulent the microbes, the less the

[1] It is, however, unsafe to declare in all cases that because a micro-organism continues to stain well therefore it was living at the moment the preparation was taken and fixed by heat. Thus in pneumonia after the crisis a fair number of diplococci may be found within the leucocytes of the expectorated contents of the alveoli, and these may stain perfectly well; yet it may be impossible to gain a single growth of the diplococcus from the same material.

proportion of them taken up by the cells, and the longer the time before the phagocytes come into action. As is the case in the unicellular organisms, so in the wandering cells of higher animals the process of destruction of the included microbes can, under suitable conditions, be seen to be digestive. Several observers have seen the anthrax bacillus, in frogs and other animals, wholly or in part surrounded by a vacuole developed within the leucocyte; and, as an evident result, the portion so surrounded has been seen to become swollen and fainter when stained, until it has undergone a veritable digestion and dissolution. By the use of appropriate reagents the vacuoles in general are seen to be faintly acid in contrast to the more alkaline surrounding cytoplasm.

FIG. 74.—Phagocytes, macrophage and microphage, to show stages of digestion and destruction of bacilli, from spleen and eye respectively of white rat with anthrax. In *1*, part of the bacillus is unaffected, but a vacuole has formed around the other part, which further has now lost the power of taking the stain. In *2*, various stages are seen, the bacilli passing through the granular, badly staining, to the vacuolated, unstained stage, until finally but faint "shadows" are observable (Zeiss, $\frac{1}{18}$, oc. 3). [METCHNIKOFF.]

As with the lower organisms, so with the wandering cells of the higher, there is an evident attraction, or chemiotaxis, whereby these cells pass towards the microbes and their products. The chemiotactic properties of the wandering cells have been especially studied by Pekelharing (78), Leber (29), Massart and Bordet (79), and Gabritchewsky (80). Of the results obtained by these observers the most important are that leucocytes are variously attracted towards various substances. Thus Leber found that the introduction into the system of finely-powdered copper and various compounds of mercury caused an abundant collection of the wandering cells around the particles, while powdered gold, silver, and iron exerted no such attraction. Gabritchewsky and A. Schmidt showed that the products of bacterial growth in general possessed chemiotactic properties yet more powerful than simple chemical compounds. While the degree of positive chemiotaxis is found to vary within wide limits, the examples brought forward of negative chemiotaxis exerted by bacterial products have so far been very few—so few as to support the contention of the late Prof. Kanthack (81), that it is very doubtful whether any microbes by their products actually repel the leucocytes, though they are capable of causing the rapid destruction of the attracted leucocytes, and so of rendering the area around the microbes relatively free from wandering cells.

This chemiotaxis would also seem in general to be in the inverse ratio of the virulence of the microbes. I say in general, for with chemiotaxis as with phagocytosis there appear to be exceptions to any uniform law: and cases can be brought forward—of diphtheria, for example—in which the leucocytes, instead of being repelled, are attracted in great numbers to the region of inoculation of a most virulent bacillus. Indeed it may be doubted whether it is the bacterial toxins as such that, diffused into

the surrounding medium, constitute the force attracting the leucocytes towards the bacteria. We now have come to distinguish two orders of pathogenetic microbes, those which during active growth give off diffusible toxins, and those elaborating toxins which during active existence are not diffused, but remain intracellular (endotoxins) (82), so that the medium in which they grow has little or no toxic effects, although if the bacteria be collected and frozen at the lowest of temperatures and then crushed, their freed body-juices are found to be extraordinarily toxic. [MacFadyen and Rowland (83).] The diphtheria bacillus belongs to the first order, forms like the B. typhosus and the cholera spirillum to the second. It is only with the death of the bacteria of this latter order that the toxins are liberated to any extent. Now as regards chemiotaxis and phagocytosis we can draw no line of demarcation between the two orders. If, therefore, as we point out, an inverse ratio can in general be detected between virulence and chemiotaxis, it is some concomitant diffusible substance, and not the toxin that attracts the leucocytes.

A very good study of the action of bacteria of different degrees of virulence can be made by repeating an experiment of Metchnikoff. The rabbit is an animal susceptible to the growth within its tissues of the bacillus of anthrax. As is well known, there are various means whereby the virulence of this microbe can be diminished; so that if cultures of the "attenuated" bacillus be inoculated into susceptible animals, these, instead of causing a fatal disease, induce but a transient local inflammatory disturbance, accompanied by fever, and followed by complete recovery. If now a small quantity of a virulent culture of the bacillus be inoculated into the one ear of a rabbit, and an equal quantity of an attenuated culture into the other, the results are very instructive. Within twenty-four hours it can be noticed that an acute inflammation has been induced in both ears; in both the vessels round the seat of inoculation are greatly congested, but whereas at the seat of inoculation of the virulent organism there is a serous inflammation so intense that the skin is raised and separated from the subjacent tissues by a clear, transparent, reddish fluid which also infiltrates the deeper tissues, in the other ear there is not nearly the same amount of swelling and serous exudation; the region of inoculation is more opaque and solid. Upon more minute examination the serous fluid in the first ear is found to contain relatively very few leucocytes; the firmer mass in the second is composed of a huge aggregation of leucocytes.

Before proceeding farther it will be well to sum up the phagocytic hypothesis of inflammation as upheld by Metchnikoff and those who see in this phenomenon the all-important factor in inflammation and the repair of injury (as also in the production of immunity), in order that, having put clearly forward the tenets of those upholding the hypothesis, I may the more readily state wherein lies the strength and wherein the weakness of the doctrine.

This hypothesis may be summed up in the following theses:—

1. That certain of the leucocytes present in the blood and lymph, notably the polymorphonuclears (microphages) and the large mononuclear hyaline cells (macrophages), are capable under certain conditions of taking up bacteria which have gained entry into the system.

2. That in addition to these, the splenic corpuscles, the cells forming the endothelium of capillaries, and other fixed cells of mesoblastic origin, possess the same property, although they exert it to a less extent.

3. That these phagocytes seize upon and destroy living and active microbes under certain conditions.

4. That the more virulent the microbe the less the tendency for the leucocytes above mentioned, and for the other fixed cells, to take up the bacteria. The less virulent the microbe the more extensive the phagocytosis.

5. That in addition to this power on the part of certain cells (the phagocytes) to take up and destroy certain bacteria, another factor has to be called in to explain why the wandering cells of the body migrate towards the focus or foci where the micro-organisms have gained an entry into the body. This factor is the "chemiotaxis" exerted by the products of bacterial growth, and by some other substances, such, for example, as the products of death of tissue and of wandering cells, and experimentally also certain chemical irritants as, for example, turpentine and mercury. In the case of the virulent microbes the leucocytes are not attracted to the focus of infection. There is a "negative" chemiotaxis, and thus, in the absence of phagocytosis, the proliferation of the microbes takes place without hindrance; whereas the less virulent microbes and their products attract the leucocytes, they exert a positive chemiotaxis, so that there is a migration of leucocytes through the capillary and venous walls to the focus of infection, and the leucocytes taking up the microbes tend to arrest the infective process.

6. That the leucocytes may become accustomed and eventually attracted to substances from which at first they were repelled, and thus a negative may be transformed into a positive chemiotaxis.

7. That the cells, having once acquired positive chemiotactic properties in relation to the products of any specific microbe, retain and transmit these properties through a series of cell-generations, the length of which varies according to the microbe, the extent of the primary reaction, and the idiosyncrasies of the individual.

8. That, consequently, the cure of zymotic or mycotic disease, whether localised or general, and immunity also, are mainly brought about by the activity of special cells (the phagocytes), and are primarily dependent upon the attraction existing between these cells and the products of bacterial metabolism.

9. The process of inflammation is essentially the endeavour on the part of the organism to promote the migration of leucocytes, and to aid the inclusion and destruction of the irritant. "The essential and primordial element of a typical inflammation is a reaction of phagocytes against the irritant (*agent nuisible*)." Or, more fully, "inflammation is

to be regarded, on the whole, as a phagocytic reaction of the organism against irritants,—a reaction which at times is accomplished by the wandering cells alone, at times with the aid of the vascular (fixed) phagocytes, or with that of the nervous system."

These are the main headings, if we may so term them, of Metchnikoff's hypothesis (for, to my knowledge, he has never formulated it clause by clause). Yet other data must be added to make it complete, data drawn from Metchnikoff's more recent studies (84), which we shall discuss in fuller detail later.

10. The destruction of microbic irritants by the cells is a process of digestion, the cells elaborate ferments (cytases) which differ in their properties; that elaborated by the microphages (polymorphonuclears) is termed by him microcytase; that by the macrophages (hyaline mononuclears), macrocytase. These ferments are the main factor in the destruction of bacteria.

11. These ferments are formed and act within the living, active cell; they are endo-enzymes. But with the death and disintegration of the phagocytes (phagolysis) they become liberated, and, through their liberation, the body-fluids become bactericidal. Since cells which are capable of acting as phagocytes liberate these cytases, the process is to be included as phagocytic.

12. It must be granted that when extracellular the cytases alone are incapable of causing bacteriolysis; bacterial destruction is brought about by the interaction of the cytase and another product of cellular activity—the "fixateur" (immune body or intermediary body). While the cytases are not specific, acting indifferently on various microbes, the fixateurs are specific, a different fixateur being developed in the process of immunisation against each specific microbe. These fixateurs are actively secreted from the living cell, and are present in the humours and exudates of the immunised animal. Metchnikoff has relatively little to say regarding these, but admits their existence, and further believes that they are developed from the same order of cells as are the cytases; hence he holds that they also are to be considered as results of phagocytic activity.

I have laid down these later theses somewhat in advance in order to present the doctrine as a whole, and that I may the more easily take up the objections that have been raised, some of which have been well met by Metchnikoff and his fellow-workers, though others still, in my opinion, have not been fully controverted.

In the terms of this hypothesis, then, phagocytosis is the all-important factor in the inflammatory process, the vascular, exudative, nervous, and other phenomena being auxiliary means whereby the phagocytic properties of the wandering and fixed mesodermal cells may be brought more fully into action: the determination of leucocytes that I have described is almost entirely to be attributed to an endeavour on the part of these cells to take up and destroy the irritant. To what extent is this doctrine to be accepted? Indubitably phagocytosis is a factor in

inflammatory processes; no antagonist of the doctrine nowadays is prepared to deny this. Nay, more, each year we recognise more fully that it is an important factor. There is not a single bacterial disease that affects man in which, to my knowledge, it has not been shown that the causative microbes are liable to be taken up by the cells, if not in man himself, at least in other warm-blooded animals. And, by repeating a very simple experiment devised by Prof. Leishman (85), this phagocytic activity of the human white blood corpuscles can very easily be demonstrated. It is only necessary to clean the finger, take a drop of blood, mix it with an equal quantity of a suspension of any pathogenetic organism, drop the mixture on a slide, place over it a cover-slip, place the preparation in an incubator at blood-heat for a quarter of an hour, then rapidly removing the cover-slip, fix the film and stain it by any good bacillary stain. Ordinary polymorphonuclear leucocytes present in the film can then be seen to have taken up, in this short time and under these not wholly favourable conditions, abundant bacteria. There may be twenty or more present in a single cell. It is when a hypothesis has been applied with the object of attaining practical ends, and is found to afford the results expected, that its value is proved, and we would point out that one of the most important recent advances in abdominal surgery has been developed from a basis of this hypothesis of phagocytosis. As already indicated, the injection of various microbic and chemical irritants into the abdominal cavity, is followed by a pronounced leucocytosis, following upon which, when particulate bodies are present, there is seen to be abundant ingestion by the cells. Taking these facts into consideration, Issaeff (86) determined that, if a peritoneal leucocytosis be induced by intra-abdominal injection of saline solutions, serums, etc., and then (twenty-four hours later) various species of spirilla be inoculated also into the abdominal cavity, the resisting power of the animal to these pathogenetic microbes is very greatly augmented. Dr. Durham (36) confirmed and showed that this was true, not only of the spirilla, but of the B. typhosus and other microbes. He found that the leucocytosis—and the increased resistance—lasted for some four or five days. Von Mikulicz and other surgeons have made use of this "Issaeff resistance period." A day prior to performing any serious operation, they inject saline solutions or serum, harmless in themselves, but capable of setting up an abundant leucocytosis. They have found that, thereby, they materially diminish the dangers of subsequent infection; the leucocytes already in the peritoneal cavity in great numbers take up and destroy bacteria which have chanced to gain entrance, before they have time to multiply.

One has but to read Metchnikoff's fascinating work on *L'Immunité dans les Maladies Infectieuses* (84), to be impressed with the extraordinary diversity and number of the researches in connexion with various pathogenetic organisms whereby the phenomena of phagocytosis have been established and confirmed. Yet, already in the course of discussion, there are one or two respects in which we are not wholly in agreement

with the general terms in which the hypothesis is set forth. (1) We doubt, for instance, the actual negative chemiotaxis—the actual repulsion from bacterial irritants. At most, with Prof. Kanthack, we are prepared to see an absence of positive attraction. This, however, is a minor point and does not seriously affect the main question. (2) We have difficulty also in recognising that the extent of chemiotaxis—and of phagocytosis—is in absolute inverse ratio to the virulence of the microbes. This obtains, we admit, in connexion with any one species; the more virulent the members of that species, the less the phagocytosis. But, comparing different species, it does not fully hold and, if virulence be dependent on toxic properties, then, when many of the most virulent bacteria do not diffuse out their toxins, we have to suppose that it is not the toxins but some other and diffusible substance, elaborated *pari passu* with the toxins, which is the cause of the attraction. Here again, while disagreeing, we do not think that this renders the hypothesis in its essence untenable. Granting this, phagocytosis might still be the all-important factor. (3) What deserves emphasis is that, by dwelling upon one function of the cells—that of phagocytosis—the hypothesis is incomplete. It is not permissible, in the first place, to expand the term phagocyte so as to include cells which do not eat, and if we agree that bacteria are destroyed and their toxins neutralised, not alone by intracellular but also by extracellular activities, substances being discharged into the lymph and blood plasma which arrest bacterial growth, neutralise the toxins, or lead to dissolution of the bacteria, then our hypothesis passes from being one of phagocytosis pure and simple into a "cellulo-humoral" one. Now we have to admit this, and, for a fuller comprehension of inflammation, have to appreciate duly all the factors that go to make up the very complicated picture. While we wholly agree with Metchnikoff that the later development of his hypothesis is a natural expansion, and while we understand the natural inclination to speak of it still as the phagocytic hypothesis, we find that the position is not clearly understood by every one, and the objection not infrequently raised that much that is now included in the hypothesis is not phagocytosis at all, is difficult to controvert in a few words. It may further be urged with some justice that the extracellular and excretory activities of the body cells are minimised, and certain other factors in the process largely neglected.

This notwithstanding, Metchnikoff's views have been purposely given this prominence. It is through him and through them, and through the active controversy and critical research initiated by these remarkable studies, that we have reached our present standpoint regarding, not merely inflammation, but the wider subjects of infection and immunity. And what is more, they are in our opinion in the main incontrovertible.

Now, in order to arrive at what we personally regard as a wider and sounder view, it may be well to detail briefly and to criticise the more important of these researches directed against Metchnikoff's hypothesis.

Chapter II.—The Humoral Hypothesis

The first strong attack—and that when Metchnikoff upheld an uncompromising phagocytosis and nothing else—was originated by Dr. Nuttall (89). So long ago as 1874, Traube and Gschleiden (88) had called attention to the antiseptic properties of the blood, and in his presidential address at the London meeting of the International Medical Congress in 1881 Lord Lister had noted that a drop of putrid blood, teeming with microbes, if diluted with a little water, when added to pure blood that had been received into a sterile vessel, might leave that blood unchanged for days, the blood remaining sweet and having, evidently, the properties of arresting the growth of the organisms of putrefaction. In 1887 von Fodor (89) of Buda-Pesth more definitely called attention to these bactericidal properties, but it was Nuttall, a Johns Hopkins student working under Flügge, whose exact studies called particular attention to the properties of the humours of the organism. In an attempt to repeat Metchnikoff's researches upon the destruction of the anthrax bacillus, this observer noticed that if he placed a fine canula containing a fresh culture of attenuated anthrax bacilli in the tissue of a rabbit's ear, there resulted in sixteen hours a rich cellular exudation; but phagocytosis appeared not to reach its maximum for twenty-two hours, and even then half of the bacilli lay free and not taken up by cells; and he found, further, that the free bacilli showed involution and degeneration to the same extent as did the ingested. This led him to study the effect of blood-serum, defibrinated blood, and lymph upon the bacilli, and he discovered that these fluids had a remarkably rapid action, destroying great numbers within a very few hours. Nuttall's very full research appeared to show conclusively that the bacteria-destroying power resided largely in the serum, and that in inflammation the exuded fluid rather than the leucocytes brought about the destruction of the microbes. Further, Nuttall found that the bactericidal substance was destroyed by being subjected for one hour to a temperature of 55° C., so that blood-serum outside the body, thus heated, lost all its powers of arresting bacterial growth. A definite, if variable, quantity of bactericidal matter was present in a given quantity of the heated serum, capable of destroying a certain number of bacteria, so that, if more than that number were added, the excess survived and, in the course of a few hours, showed active multiplication. These observations were confirmed and extended by Nissen (90), Behring (91), and Buchner (93), and a most valuable series of contributions have been made by Dr. Hankin (92), Buchner, Vaughan (94), Tizzoni and Cattani (95), Behring, Ehrlich and his pupils (96), and others, upon the nature and properties of the substances to be derived from the blood-serum of animals either naturally immune to certain diseases, or rendered immune by one or other procedure. What is more, it has been recognised that two orders of substances are recognisable; one capable of destroying pathogenetic microbes,

the other not destroying them, but rendering their products inert. We cannot here give these important observations in detail (84), as they bear more particularly upon the subject of immunity. It was shown from several sides that, in the blood-serum and removed body-fluids as also under certain conditions within the tissues, there occurs active destruction of bacteria without the bacteria being ingested by the cells. The experiments were so clear, so easy to repeat and confirm, that we can well remember the time when, to believe in phagocytosis, even as an auxiliary process in the arrest and cure of disease, was to be regarded as to be lacking somewhat in common sense. The destruction of bacteria in the economy was held to be almost entirely—in some cases entirely—brought about by the action of the humours of the body.

But this humoral hypothesis pure and simple was soon seen to be inadequate. Its upholders could not say how and whence the bactericidal substance was derived, and the more sera were studied—whether gained from healthy animals, from individual cases of the disease, from animals naturally immune to certain diseases, or those rendered immune by inoculation of this or that microbe—the more impossible it became to recognise any sure relationship between the bactericidal power of the serum and the extent of resistance displayed by the individual affording that serum. It was noted also that the different humours of the body differed in bactericidal properties in a way that could not be adequately explained in the terms of this hypothesis.

Chapter 12.—The Cellulo-Humoral Hypothesis

If the serum and if the blood-plasma contain bactericidal substances, these must in all likelihood be developed by certain cells, and thus at bottom the humoral conception must be cellular; and the very fact of the great increase in the bactericidal properties of the blood immediately on its withdrawal from the body, must suggest that in the changes which occur in the extravascular blood there is a liberation and solution of bactericidal substances. Now the first and foremost of these changes is the breaking down of the leucocytes as the blood begins to clot. It may, therefore, be that this breaking down of the leucocytes, with liberation of their contents, is capable of explaining the increased bactericidal action of defibrinated blood and blood-serum. This, let me repeat, is not phagocytosis, at most it is a function of cells which can act as phagocytes. If correct, it seems that that group of wandering cells which more particularly exhibit phagocytic properties is also able to bring about the destruction of bacteria and the neutralisation of toxins by other means. As a matter of fact, evidence has steadily accumulated showing that more particularly the wandering cells of the body and also, probably, certain orders of fixed cells possess these other means. Many years ago Ribbert (98), in his studies upon the fate of spores of sundry species of mould (aspergillus and mucor) inoculated into

the anterior chamber of the rabbits' eye, had found that two stages of reaction were to be made out; at first the spores and developing hyphal filaments became surrounded by dense clusters of leucocytes which remained in apposition to but did not ingest the micro-organisms. They appeared to bring about a weakening and lowering of vitality on the part of the spores and filaments, so that, after a time, other cells wandering into the part could manifest their phagocytic action and take them up. Ribbert, it is true, attributed the lowering of vitality to the walling-in ("Wallbildung") of the leucocytes and consequent lack of nutrition. The fact remains that he demonstrated a preparatory extracellular action upon the micro-organisms by the leucocytes.

That the leucocytes contain bactericidal substances was first demonstrated by Dr. Hankin (92), who obtained from the lymphatic glands and spleens of animals immune to anthrax (dogs and cats), a proteid of the nature of a globulin, identical with Prof. Halliburton's cell-globulin β, and having a bacteria-killing power similar to that possessed by blood-serum. In later observations upon the rat he showed that there was a relationship between the amount and activity of these "defensive proteids" and the power of resistance of the animal to the disease. Thus Dr. Hankin showed that in animals possessing the power of destroying bacilli, the organs containing the largest collections of leucocytes yielded notable quantities of a bacteria-destroying substance. These defensive proteids are now more commonly known as alexins, this name having been given to them by Buchner, who, beginning as a strong supporter of the humoral hypothesis, ended in assuming a position which more nearly approached that of Metchnikoff. It was shown by Denys and Havet (99), of Louvain, that exudates rich in leucocytes have a more intense bactericidal power than has the blood-serum of the same animals, and that the blood and exudations of the dog freed from leucocytes, either by infiltration or by centrifugal action, lose their bactericidal power, regaining it when the leucocytes are re-introduced. Buchner (93) fully confirmed these observations. He showed that, if sterilised emulsions of the gluten of wheat be injected into the pleural cavity of a dog or rabbit, its presence leads to the pouring out of an aseptic exudation peculiarly rich in leucocytes, and this exudation is much more bactericidal than is the blood or the serum of the animal. He noted further that, like the alexins of blood-serum, this bactericidal substance of inflammatory exudates is destroyed by heating to 55° C. Several other observers (Bail (101), Schattenfroh (102), Van der Velde (103), Jacob (104), Löwit (105), and Bordet (106)) have obtained similar results, employing various methods. Thus it is now generally accepted that the alexins or bactericidal substances of the serum, as of exudates, are derived very largely from the leucocytes, and that when, therefore, bacteria undergo destruction in the humours of the body without the intervention of cells, that destruction is indirectly due to the leucocytes.

Yet another line of work independently points in the same direction. Vaughan (94) separated from blood-serum nuclein, a body which so far

had been found exclusively in connexion with the nuclei of cells. This nuclein is either itself bactericidal or has a bactericidal substance in association with it. The presence of such a body in the serum is best explained by the disintegration of nucleated cells, *i.e.* of leucocytes.

Clearly then leucocytes of certain orders contain bactericidal substances; can we recognise not merely a liberation of anti-bacterial substances by disintegrating leucocytes, but a functional active secretion of the same such as has been held by the late Prof. Kanthack and Mr. Hardy, and by Buchner and his school? Metchnikoff largely denies this; the microcytase and the macrocytase, the digestive ferments of the two main orders of leucocytes, are, according to him, endo-enzymes, acting with the cell-body and only discharged with the dissolution of the cell. At a very early period it was shown by Nuttall that the blood-serum removed from the body acts far more rapidly and energetically than does the blood-plasma and lymph within the body. The disparity of action between the two is remarkable. Thus Lubarsch (107) has shown that in order to kill a rabbit by intravenous inoculation of anthrax bacilli into the circulating blood, at least 16,000 virulent bacilli must be introduced. In other words, the whole circulating blood is able to destroy only some 16,000 bacilli at a time. On the other hand, a single cubic centimetre of the blood serum derived from such a rabbit can, outside the body, kill an even greater number of bacilli in a few minutes. The normal blood-plasma, therefore, does not appear to be actively bactericidal, and this is confirmed by certain striking observations by Gengou (108). If rabbits' blood be obtained with every precaution against admixture with the body-fluids, be received into paraffined test-tubes, and be centrifugalised immediately so as to remove all the cells, a serum or plasma is obtained which will remain liquid for several days. So obtained, there has been a minimal breaking down of the leucocytes. This plasma has practically no bactericidal properties, but, on the contrary, serum from the same animal, obtained from blood allowed to clot, is actively bactericidal. In this process of clotting there is, as we know, an extensive destruction of leucocytes.

But Gengou's experiments merely demonstrate that in the normal animal not subjected to bacterial invasion the leucocytes circulating in the blood do not actively discharge bacteriolytic substances into the plasma: they do not controvert the possibility that, under bacterial stimulus, the cells of the body actively secrete these bacterial substances. It is, we confess, difficult either to prove or disprove that this is the case. If bacteria or their products be injected into the body-fluids, and these are found to become increasingly bacteriolytic, it may well be urged that the result is wholly due to resulting disintegration of the leucocytes.

Pfeiffer's Phenomenon.—A few years ago proof positive of such exudation, not by leucocytes, it is true, but by endothelial cells, seemed to have been discovered by Pfeiffer of Berlin (109). If a few drops of a pure culture of the cholera spirillum be injected into the peritoneal cavity of a guinea-pig, vaccinated against cholera, and, a few minutes later some

of the peritoneal fluid be examined, it is seen that very few leucocytes are present, and, this notwithstanding that the spirilla, instead of having their usual curved "comma"-like form, have become globular, the majority staining badly and being dead. Outside the body the blood-serum of a highly immune guinea-pig has similar properties. If heated to 55° C. for an hour these properties are lost. There is, therefore, present in the peritoneal fluid, as in the blood-serum, a body of the nature of an alexin which clearly is, to some extent, responsible for this remarkable alteration in the spirilla.

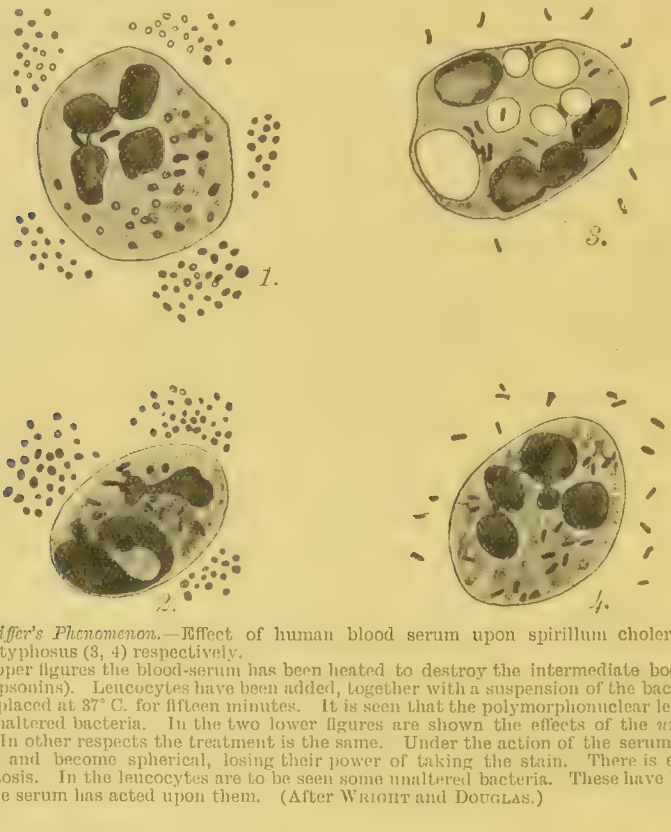

FIG. 75.—*Pfeiffer's Phenomenon.*—Effect of human blood serum upon spirillum choleræ (1, 2) and Bacillus typhosus (3, 4) respectively.
In the two upper figures the blood-serum has been heated to destroy the intermediate bodies (immune bodies, opsonins). Leucocytes have been added, together with a suspension of the bacteria, and the mixture placed at 37° C. for fifteen minutes. It is seen that the polymorphonuclear leucocytes take up the unaltered bacteria. In the two lower figures are shown the effects of the *unheated* blood serum. In other respects the treatment is the same. Under the action of the serum the bacteria swell up and become spherical, losing their power of taking the stain. There is equally active phagocytosis. In the leucocytes are to be seen some unaltered bacteria. These have been ingested before the serum has acted upon them. (After WRIGHT and DOUGLAS.)

It is impossible to deal in detail with the important controversy that has raged regarding the meaning of this Pfeiffer's phenomenon. Suffice it to say that Pfeiffer regarded the substance causing the phenomenon as an excretion from the peritoneal endothelium; that Metchnikoff demonstrated that it was best explained by what he has termed "phagolysis"—by the rapid clumping of the leucocytes of the peritoneal cavity upon the omentum, followed by their dissolution and liberation of bactericidal substances; he has shown further that the phenomenon does not develop in connexion with body-fluids, such as the aqueous humour, containing few or no leucocytes; and that it does not occur if phagolysis be

prevented; while Bordet (110) demonstrated that the reaction needed the presence of two substances—an alexin or microcytase derived from the broken-down leucocytes, which is destroyed by heating to 55° C., and a second substance, not present in normal animals but present in the serum and peritoneal fluid of vaccinated animals, which is only destroyed at a temperature of 68 to 70° C. This substance belongs to the group of bodies which have been termed fixateurs, immune bodies, intermediary bodies, etc. In short, says Metchnikoff, it is the breaking down of the peritoneal leucocytes that is the main factor in bringing about Pfeiffer's phenomenon. But where does the second substance, the intermediary body, which also is essential for the development of Pfeiffer's phenomena, come from? It is present, not only locally, but in most of the body humours. To be brief, there is no evidence that this substance is, under normal conditions, purely intracellular. The evidence, so far as it goes, is all to the contrary. As with the allied group of substances known as the agglutinins and the whole group of immune bodies produced in the development of immunity, these fixateurs or intermediary bodies are widely distributed in the organism, even in the excreta of immunised animals. They appear to be actively produced, and that over relatively long periods, and so we must conclude that they are products of living cells. This, at least, is the view accepted by all who have studied them, and, though he has singularly little to say regarding them, Metchnikoff's view partakes of this opinion (*vide* 84, p. 816). He regards them as also, in the main, produced by those cells which, under other conditions, act as phagocytes. This is, to say the least, doubtful. As Dr. A. E. Wright (111) points out, the organisms which exhibit Pfeiffer's phenomenon under favourable conditions—notably the spirillum of cholera and the B. typhosus—may be taken up by the peritoneal leucocytes very rapidly, before the phenomenon has manifested itself. When so taken up, they do not swell up and become globular, though others, ingested later, have a globular appearance. If the phagocytes themselves produce the intermediary substance, why should not the bacteria undergo like alteration *within* the bodies of the phagocytes? It is only outside these cells that the change takes place.

Wright's Phenomenon.—Where, indeed, these intermediary bodies are produced is, at the present time, an open question. That they play an important part is most evident, but, what is more, the recent observations of Drs. Wright and Douglas (111) show that, in connexion with the majority of pathogenetic bacteria, phagocytosis occurs with difficulty, if at all, in the absence from the body-fluids of certain of these intermediary bodies. These particular ones they have termed opsonins. Dr. Wright and his fellow-workers confirmed the observation of Drs. Nuttall, Stern, and others that blood-serum has no bactericidal affect upon the pyococcus aureus. They were thus led to investigate to what extent active phagocytosis might explain the destruction of pyococci gaining entrance into the organism, and found that an active phagocytosis occurred, but only under certain conditions. If, by centrifugalisation, the corpuscles are

separated from the blood, and now a mixture be made of the washed white blood corpuscles, the serum, and a suspension of the pyococci, and this mixture be kept for a quarter of an hour at the temperature of the blood, active phagocytosis occurs; the polymorphonuclear leucocytes are seen to contain, each of them, numerous cocci. But if now, before making this mixture, the serum be heated to 65° C. and then added, there is little or no phagocytosis. This points to the existence of something in the unheated serum which favours the process of ingestion of the bacteria, and, as a matter of fact, they show that a component of the active serum has a preparatory action upon the suspended bacteria, so that bacteria subjected to an unheated serum for a time and then placed in the heated inactivated serum are taken up more readily than those placed direct into an inactivated serum. They show, further, that in the process of rendering an individual more refractory to pyococcic infection, his serum comes to contain increasing quantities of this opsonin or intermediary substance. So that, taking the washed white blood corpuscles of an ordinary individual, adding these to a mixture of the serum of the immunised individual with a suspension of pyococci, the leucocytes of this *normal* individual take up a much greater number of the cocci in a given time than do washed white blood corpuscles of the *immunised* individual suspended in the centrifugalised serum of the normal individual, to which a culture of pyococci has been added. What is true of the staphylococci obtains also with the long series of other bacteria, the only exception noted being in connexion with members of the diphtheria group. These opsonins are found to be distinct from alexins or bactericidal substances, apparently distinct also from the ordinary intermediary bodies, for their activity is greatly lowered by subjection to a temperature of 55° C. But, as with the intermediary bodies, it seems improbable that they are secreted by the phagocytic cells. Drs. Wright and Douglas found that the blood-serum of cases with abscesses might be from six to ten times more active in promoting phagocytosis than the serum extracted from the pus of the abscesses. If leucocytes secreted these substances, then we should expect that, in collections of leucocytes, the reverse should hold good.

Here then phagocytosis is shown to be a most important factor in the destruction of bacteria, but another must also be included, *i.e.* the presence of a substance not derived, it would seem, from the cells actively involved in the phagocytic process. It is interesting to note that the late Prof. Kanthack and Mr. Hardy (37), whose observations I quoted in a previous edition of this article as affording direct evidence that the leucocytes secreted bactericidal substances, were the first to demonstrate clearly the compound nature of the bacteriolysis. Adding a suspension of anthrax bacilli to frogs' lymph and studying what happened, by prolonged examination under the microscope, they observed that cells possessing granules staining with eosin (amphophil cells) attacked the bacilli, coming into contact with them, and, in this process, the granules were seen to be discharged. These cells did not actively ingest the bacilli, but

they, while remaining extracellular, showed evidence of degeneration. Only later and by another form of leucocyte was there, in the frog's lymph, active phagocytosis. In other words, according to them, one set of leucocytes secreted the substances acting upon the bacilli, and prepared these to be ingested by another order of these cells.

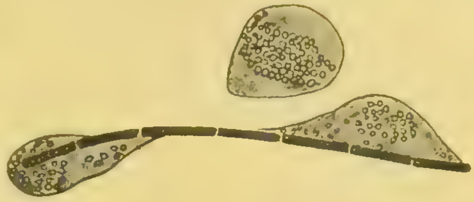

FIG. 76.—Granular (oxyphil) leucocytes attacking and coming into apposition to chain of *B. ramosus*. From a Ziegler's chamber preparation, peritoneum of guinea-pig. (KANTHACK and HARDY.)

It must be admitted that these observers introduced not a little confusion by speaking of this first order of leucocytes in the frog as eosinophil cells. As a matter of fact, these cells correspond in most respects to the neutrophil and amphophil polymorphonuclears of the mammal, to cells which in higher animals are definitely phagocytic. Mesnil and others have been unable to confirm these observations; but then they have not repeated Prof. Kanthack and Mr. Hardy's experiments according to the lines laid down by them; they have attempted other methods. It must be admitted that in the frog the experiment does not always succeed. I have, however, made and seen preparations in which this loss of granulation and coincident degeneration of the bacilli could not be denied. We have not been able to convince ourselves that in the mammal the coarsely granular eosinophil possesses a like excretory function, although Prof. Kanthack and Mr. Hardy convinced themselves that this was the case. The observations of Dr. Durham and others indicate a little-understood alteration in bacteria preparatory to ingestion, which would suggest that the leucocytes of mammals afford some preparatory secretion. If, for example, a relatively abundant suspension of actively motile but not highly virulent bacilli be introduced into the peritoneal cavity of an untreated guinea-pig and a drop of the peritoneal exudate be examined, it is noted at a certain period that while many of the bacilli are moving freely in the fluid, and may impinge upon the hyaline mononuclear cells present with impunity, those that come into contact with the polymorphonuclears become arrested and motionless, and the individual leucocytes may be seen taking on a "hedge-hog" appearance, the immobilised bacteria adhering by one end to the leucocyte. This adhesion and immobilisation, prior to ingestion, cannot, I think, be

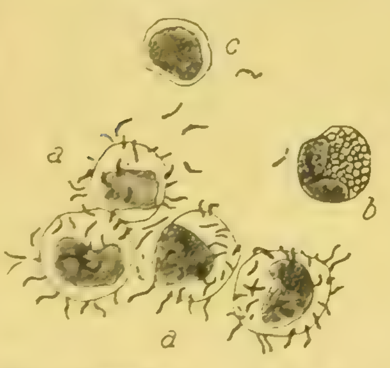

FIG. 77.—Leucocytes from peritoneal cavity of guinea-pig into which a microbe of low virulence (Sanarelli's "Versailles" vibrio) has been inoculated, to show "hedgehog" appearance around the mononuclear leucocytes (a). The eosinophils (b) and the lymphocytes (c) were not affected (the polymorphonuclears — not shown — to a less extent than the hyalines). (After DURHAM.)

explained except by presupposing the existence of a zone of diffusible material discharged from these cells and having a preparatory action upon the bacilli. Putting all the facts together, it would seem that, under certain conditions, some preparatory or intermediary substances are separated from leucocytes of one or other order which aid in the process of phagocytosis, but the evidence is very far from conclusive that all the preparatory substances are of leucocytic origin.

Chapter 13.—Summary

I am thus led to modify Metchnikoff's conception of the mode of action of the leucocytes to some extent, and to believe that the following more nearly represents the state of our knowledge.

(1) Phagocytosis—the process of ingestion and digestion on the part of the cells of the organism—is the factor most generally involved in the destruction of pathogenetic organisms within the system; both fixed cells, like those of the endothelium, and certain orders of free cells—leucocytes can manifest this property.

(2) Where the cells are able to take up living bacteria, these cells have, in most cases, to be subjected to an extracellular action by substances present in the surrounding medium (opsonins) prior to digestion.

(3) Bacteria may also undergo destruction without phagocytosis taking place. Where this is the case, the bacteriolytic substance (cytase) is liberated into the medium upon the death and disintegration of cells that are potentially phagocytes. It, however, cannot act without the intervention of a second intermediary body (fixateur) present in the medium.

(4) Whether leucocytes and other cells of the body can actively secrete the bacteriolytic substance when stimulated, must be left an open question; it must, however, be recognised that certain leucocytes secrete and discharge substances which, if not directly bacteriolytic, are preparatory to and essential for the destruction of the bacteria.

I have so far utilised Metchnikoff's terminology, using the term "cytase" for the intracellular bacteriolytic substances and, thereby, tacitly accepting the view that these bodies are ferments (the termination "-ase" being the conventional method to signify an enzyme). This is the view of the French school of bacteriologists generally. How far is this accurate? Other workers are by no means convinced that this is their nature. Pfeiffer and Ehrlich[1] regard the intermediary body or amboceptor as the ferment; and there is much to be said in favour of this view, but, so long as the nature of enzyme action is not clearly understood, so long as it is currently accepted that, in organic fermentations, only two factors are involved, for so long must there be confusion

[1] "Da unter dem Einfluss des Addiments (*intermediary body*) Erscheinungen auftreten, die man mit Pfeiffer als der Verdauung analog ansehen muss, so werden wir nicht fehlgehen, wenn wir dem Addiment dem Charakter eines Verdauungsfermentes vindizieren."—Ehrlich und Morgenroth. *Ueber Haemolysin.* 1. Mitteil. *Gesammelte Arbeiten von Ehrlich*, p. 12.

regarding what is the true ferment or enzyme. As a matter of fact, it would seem that in all organic enzyme action for the development of the complete cycle there are at least three factors requisite, and we have to decide which of these three is the ferment. The realisation that three factors are and must be involved immediately aids our comprehension of the facts here brought forward, and renders it easy to grasp the otherwise most puzzling order of affairs presented in the co-existence and mutual action of the amboceptors and complements, of fixateurs and cytases, opsonins, lysins, *et hoc genus omne.*

The ferments of the body should not be looked upon as a special group of chemical compounds, but, on the contrary, enzyme action should be viewed as a property of a series of substances possibly of very different chemical composition. This view was seriously discussed by Professor Woodhead (112) many years ago. The study of the catalytic action of finely divided platinum, of manganese dioxide, etc., supports this view. The ferments, or bodies presenting enzyme action, may be regarded as a

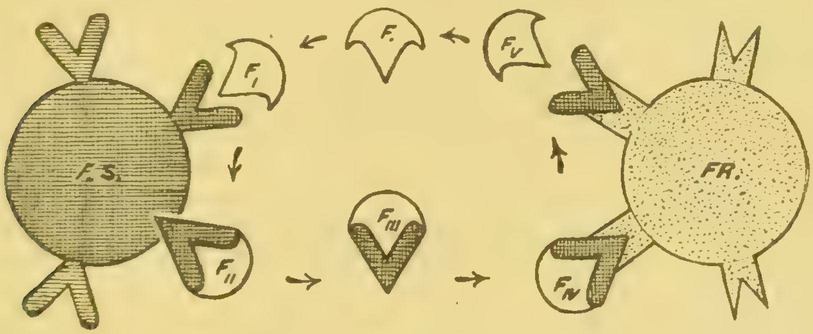

Fig. 78.—Diagram to illustrate the conception regarding ferment action and its application to the side-chain hypothesis of immunity. *FS*, molecule of fermentescible substance with side-chains; *FR*, molecule of fermentator; *F*, ferment; F_I F_{II}, etc., the successive stages in the action of the ferment.

certain order of unsatisfied molecules, which enter into combination with certain other molecules in the surrounding medium for which they have affinity; a chemical action takes place resulting in the enzyme becoming attached to certain atom groups of the fermentescible molecule. It is not even necessary to suppose that as the result of this chemical action, the atom groups are immediately detached. So soon as this union takes place, the enzyme molecule becomes satisfied, and, were there no other substances present to disturb the equilibrium, further action would cease. For ferment action to continue there must be some third substance present, which we may term the fermentator or complement, having an affinity for the atom group represented by the ferment plus side-chain, or atom-group, of the fermentescible substance. As the result of its presence, a second union takes place, and what had been the unsatisfied atom-group of the fermentescible substance of the above compound, becomes now attached to and combined with the fermentator. The ferment becomes free, once more unsatisfied, and ready to act again on the fermentescible substance. We may go farther and suppose that the

atom-group or side-chain of the fermentator thus modified by combination with the atom-group from the fermentescible substance, may either remain attached to the fermentator (complement) or become liberated as a separate entity.

According to this conception of ferment action, which is the ferment—the intermediary body (fixateur) or the lysin, complement or cytase? Clearly, I think, the former; the cytase can only be regarded as the fermentator, the substance essential for the final act in the process. And this view is supported by Dr. Wright's phenomenon, in which the bacterial bodies must have the intermediary body (opsonin) in association with them before they can be acted upon by the cells. Possibly it is a matter of convention which we shall term the enzyme or ferment, whether the intermediary body or the third substance essential for the completion of the process. Yet it seems more just that the active factor in the process should receive the name; just as, with Pawlow (113) and Drs. Bayliss and Starling (114), and in opposition to Metchnikoff and Delezenne (115), I would lay down that in tryptic digestion the enterokinase is the true ferment, and would regard the trypsinogen as the fermentator. And thus, to sum up, I find myself in harmony with Pfeiffer and Ehrlich in regarding the amboceptor or intermediary body as the ferment, and, in place of speaking of the cytase of the phagocytes, would speak of the cytolysin or the bacteriolysin.

To complete this section I will here add other conclusions deduced from a study of the later stages of inflammation and discussed in a later chapter ("Upon the part played by the fixed cells in the Inflammatory Process"), viz.:—

1. In the later stages of inflammation the growing fibroblasts may often be seen to contain leucocytes in process of digestion. Presumably, therefore, a certain number subserve nutrition.

2. Others are, in certain cases, recognisable in the lymph-spaces outside the inflammatory focus, containing the debris of dead tissue. Emigration can therefore occur as well as immigration.

3. The process of development of wandering into fixed cells has been observed; cells of what are here termed the hæmatogenous type have never been observed to become thus converted; the histogenous alone would seem able to undergo the change.

4. The contrary process of development of wandering cells from degenerating tissue (muscle-fibres) has also been recorded by more than one observer.

II.—The Inflammatory Exudation

Chapter 14.—The Fluid of the Exudate

Whenever injury to the tissues leads to vascular dilatation there is an increased effusion of fluid from the blood. The extent of this effusion

varies greatly; it varies with the tissue affected, the state of the organism, and the quality and nature of the irritant. Dense tissue permits of little exudation, while loose vascular tissue, under the action of an irritant of no great intensity, may undergo great exudative swelling. There is, for instance, a peculiar liability in serous and cutaneous surfaces (or more truly in subserous and dermal layers), when inflamed, to manifest abundant exudation. Their vascularity and the slight external resistance would appear to explain this liability. There is a like tendency to abundant exudation from mucous surfaces, though here to a large extent, so long as the covering epithelium is not destroyed, the exudation is governed—*i.e.* partakes of the nature of an excretion, abundant mucus from the cells being also discharged, and is not extreme. With destruction of the covering epithelium it may become profuse; choleraic diarrhœa is perhaps the most pronounced case of exudation in the human organism. That some general state of the organism is a factor concerned is seen when virulent anthrax bacilli are inoculated subcutaneously into an ordinary rabbit and into one that has been rendered immune: in the former the exudation is of a serous nature, in the latter little fluid is exuded from the vessels—a clear indication that, in the development of the immune state, not merely the leucocytes, but also the capillary walls, at the least, become altered in their behaviour to the toxins. The effect of the quality of the irritant is observable upon comparison of the results of inoculation of various microbes. Some cause little exudation of fluid. These are in general of low pathogenetic quality, but not always; certain virulent microbes (such as those of tetanus) lead, when inoculated, to relatively little effusion of fluid from the vessels. On the other hand, it may be stated definitely that where in a moderately dense tissue the injection of a pure culture of a micro-organism leads to well-marked exudation, the micro-organism is of high virulence.

Can any meaning be ascribed to this effusion, or, to express the same idea in words which shall not offend those who fear the semblance of teleological ascriptions, has the increased pouring out of fluid into the tissues as the result of irritation, been of proved benefit to the species, so that those individuals have survived who have manifested this reaction and have conveyed it to their offspring? Is it an attempt at increased nutrition in the injured region? It has been suggested, in accordance with Virchow's conception of inflammation, that the injury, stimulating the surrounding fixed cells, leads to increased local metabolism; and that the exudation is a means of bringing to the region the increased nourishment demanded by the increased cellular activity. But inasmuch as exudation is most marked in those cases where there is most profound and rapid cell destruction, and again at the early stage of the inflammatory reaction, when evidences of growth and proliferation of the fixed cells of the region may be, and most often are, wholly wanting, this view can scarcely be upheld. Yet at a later period of the process, and again in chronic inflammation, the overgrowth of the connective tissue-cells would appear to stand in some relationship to the over-nutrition caused by the

continued dilatation of the vessels and the pouring out of excessive lymph into the tissues. It must, however, be admitted that the exact relationship subsisting between nutrition and cell overgrowth is still a matter of debate among pathologists.

That the exudation exerts a "flushing-out" action is very evident in many cases. Thus the inflammation induced by plunging an animal's leg into hot water is accompanied by great increase in the amount of lymph obtainable from the efferent lymphatics of the part. Experimentally it may be shown (Samuel (116) and others) that seven to eight times as much lymph may drain away from an inflamed as from an uninflamed region. It is shown also by the presence of streptococci in the lymph channels outside the area of acute inflammation in erysipelas, by the frequent implication of the nearest lymph-glands in suppurative disturbances, and by the appearance of lesions, due to the direct action of bacterial products, in organs far removed from the focus of bacterial proliferation in such diseases as diphtheria and tetanus, wherein, as a rule, the bacteria remain strictly localised. It is clear that the exudation into an inflamed area may be much in excess of the normal transudation; that it can accomplish a removal of irritant matters. It is clear also, from more than one of the examples given above, that a process which may be beneficial to the region of injury may be harmful to the system as a whole.

Study of the "flushing-out" effects of the inflammatory exudate affords, in fact, a good object-lesson as to how far the reaction to injury is to be regarded as purposive. Yet we are forced to see that there is a certain amount of adaptation. Where the irritant can be conveyed to the exterior an abundant exudative inflammation generally occurs—an abundant flushing; where it can be conveyed into one of the body cavities the same holds good; but here a mechanism is often called into action whereby the exudate with its contained irritants is held within the serous cavity for days and weeks after all signs of active inflammation have subsided. The organism, that is to say, would seem to restrain its drainage to the general lymphatic system. Where the irritant is merely the product of tissue-change the profuse exudate is rapidly conveyed away; where, on the other hand, the injury is of bacterial origin, the passage of lymph from the focus of inflammation, is, generally speaking, not nearly so free; it is of thicker consistency and drains away slowly. In short, as I have already indicated, where the microbe is not too virulent a cellular rather than a serous inflammation is produced; and in place of abundant flushing an increased antibacterial and antitoxic action of the exuded lymph comes into play.

But besides the mere "flushing-out" the exudation has often another effect, namely, dilution of the irritant and reduction of its injurious properties, so that it acts with lessened force upon the tissues, and permits the wandering cells to be attracted to the region where they may exert their functions. Where a comparatively mild physical irritant leads to abundant exudation the flushing-out action appears to be in the ascendant,

where microbic irritants cause great local inflammatory œdema, judging from the less extensive lymph flow from the region, the diluent action must be regarded as the more important. I have already pointed out that a relation may be traced between the intensity of bacterial irritation and the extent of the exudation. In short, there may be great exudation under two apparently opposed conditions: in the presence of comparatively mild physical irritants, and in that of severe bacterial irritants. In the former case it more especially subserves removal, in the latter dilution of the poison.

Chapter 15.—The Solids of the Exudate

The fundamental characteristic of inflammatory exudation as compared with ordinary lymph is its richness in proteids. Whether we regard lymph as a filtrate pure and simple from the blood, or follow Heidenhain in regarding it as the result of a selective filtration, it is highly probable that in inflammation the exudate approaches in its composition more nearly to the blood-plasma than does ordinary lymph. The dilatation of the capillaries, the consequent thinning of the endothelial layer with, it may be, the opening of some lacunæ between the individual cells, and the direct action of the irritant upon these cells, may all be expected to aid the transudation. In this way the amount of proteid matter in the lymph may be increased. But equally important must be the addition of proteids due to the breaking down of leucocytes and tissue-cells. I have already discussed this destruction of the cells, and need not here give the evidence of its occurrence.

This increase in the solids, mostly proteids, of the exudate, has been well shown by Samuel, by measuring the flow of lymph from the main lymph-channel of the dogs' foot. In one such experiment he found that there was discharged in successive periods of three hours:—

1. Untreated foot; 4·0 c.cm. lymph containing 4 to 5 per cent solids.
2. Foot subjected to venous obstruction; 28·5 c.cm. of lymph containing 2 to 3 per cent of solids.
3. Foot inflamed; 28·5 c.cm. of lymph containing 7 per cent of solids.

The figures in the third case—of inflammation—do not represent the whole exudate. So thick was the lymph that it tended to clot and obstruct the canula, and there was, in addition, much œdema and swelling of the foot. But obviously, as Dr. Ainley Walker (117) points out, from twenty to thirty times more proteid matter may drain away from an inflamed than from a healthy region.

In addition to the proteids the inflammatory lymph may contain other substances worthy of more than passing note. Of these the more important are ferments, the results of proteolysis (notably fibrin and its precursors, nucleo-albumins and albumoses), and in many cases mucin, together with bactericidal substances, and, where bacteria are present, the products of their growth. Various extractives have been noted. Exudates

rich in cells and disintegrated tissue-products—pus, for example—may contain glycogen, fats and, as Dr. Klotz working in my laboratory at McGill University has recently shown, a very definite amount of soaps.

The presence and amount of these substances depend largely upon the intensity and character of the inflammation. Thus the total quantity of proteids, and the proportion of fibrin, albumin, and globulin present, vary within wide limits. The following table[1] of observations made by Professor Halliburton (122) shows well this variation in proteids, and the difference existing between inflammatory exudations and dropsical effusions :—

Pleural Fluid from	Sp. Gr.	Percentage Quantity of			
		Total Proteid.	Fibrin.	Serum-globulin.	Serum-albumin.
Acute pleurisy, Case 1	1023	5·123	0·016	3·002	2·114
,, ,, Case 2	1020	3·4371	0·0171	1·2406	1·1895
,, ,, Case 3	1020	5·2018	0·1088	1·76	3·330
Hydrothorax . . Average of three cases	1014	1·7748	0·0086	0·6137	1·1557

Exudates, as a rule, have an acidity above 10 with decinormal soda solution, using phenol-phthalein as an indicator, transudates under 10. The difference is too slight to be relied upon. Reuss, Hofmann, and others have shown that the amounts of solids and extractives vary very slightly; it is the albuminous matters which mainly determine the variations in the specific gravity. The factors determining the amount of albumin are many. Thus, as a general rule, more albumin will be found in a pleural exudate than in a peritoneal exudate. Some observers, however, place peritoneal exudate first in order. The pericardial and the subcutaneous come next. It has been noted, further, that the specific gravity and amount of albumin are somewhat higher in right-sided pleurisies than in left (Berheim and Brunting). The amount of albumin in the blood is also a factor. Thus in anæmia or hydræmia, the specific gravity of exudates is lowered. Other factors are also given ; among them the not unfrequent combination of mechanical effusion—or obstruction—with active inflammation. The most important of all would appear to be the extent of irritation of the affected part. Thus, in four cases of pleurisy, Runeberg compared the amount of albumin found in the pleural fluid with that present in acute blisters produced on the patients by cantharides ; the average of the former was 5·43, of the latter 6·2 per cent ; without exception, the percentage in the blister-fluid was found the higher. It may be laid down (Miller) that fluids with the specific gravity of 1018 or higher, with at least 4 per cent of albumin,

[1] These figures are thoroughly in accord with those of other analyses by Reuss (118), Hofmann (119), Mehu (120), and Letulle (121).

are of inflammatory origin; or from 1010 to 1015, with albumin up to 3 per cent, are due to venous stasis; of less than 1010, with albumin under 1 per cent, are due to hydræmic conditions.

The Cells of the Exudate.—Much study has, of late years, been devoted to cytodiagnosis, to the diagnosis of inflammatory and other conditions by a study of the cells present in the removed fluids. It cannot, however, be said that, for our present purposes, much has been elicited beyond this, that abundant polymorphonuclears indicate an active inflammation; a preponderance of lymphocytes, either a tuberculous infection or sub-acute inflammation of other nature of some little duration, though it has also been noted that in the early stages of a tuberculous inflammation (*e.g.* in a rapidly developing tuberculous pleurisy) there may also be an abundance of polymorphonuclears.

Fibrin.—Between the amount of fibrin present in exudations and the amount of peptones there is an inverse ratio. Peptones are especially developed in connexion with suppurative inflammation; and the more an inflammation tends to be suppurative the greater is the breaking down of the fibrin, as also of fixed and wandering cells, and the more evident the production of peptones or more correctly of albumoses, until in chronic abscess-formation of fair extent these pass into the general circulation, and are excreted and recognisable in the urine.

Into the discussion of the mode of formation of fibrin I need not enter here, intimately connected as the subject is with the inflammatory process. The greater textbooks of Physiology enter exhaustively into the matter. Suffice it to say that, as in the blood, a direct relationship is made out between the breaking down of leucocytes and the development of this substance in inflammatory exudations.

It is in connexion with inflammation affecting serous and epithelial surfaces[1] that fibrin is more clearly recognisable, forming, it may be, thick coatings of the badly named "inflammatory lymph" over the inflamed surfaces. This deposit is in all respects comparable to the formation of thrombi in the blood-vessels. [*Vide* article upon "Thrombosis."] Here, as there, the deposit occurs only when the endothelium has undergone destruction and the roughened sub-endothelial tissues are exposed. And here also the fibrin may be deposited either in filamentous or homogeneous and hyaline form according to circumstances. How far the blood-platelets are involved in the production of inflammatory fibrin is a matter deserving further study.

The above statement gives the general consensus of opinion among pathologists of the present time regarding the mode of origin of inflammatory fibrin. And yet this view has been vigorously opposed by Neumann (123), at least as regards pseudo-membranous inflammation. According to him, careful examination of fibrinous inflammation of the serosa and of diphtheritic inflammation of the mucous membranes shows that the deposit of fibrin does not lie upon, but under, the endothelium

[1] Of epithelial surfaces, more especially those covered by a single cell layer, as notably the pulmonary alveoli.

or epithelium. The statements of other observers (Marchand (124), Orth (125), Ziegler (126)) that endothelial cells can be seen here and there still remaining under the fibrin, he strongly controverts; the cells so seen are, he declares, swollen connective-tissue cells, and the hyaline glistening bands of fibrin are seen to be directly continuous with the connective-tissue fibrils; the bands of fibrin, in short, are derived from, and are a modification of, the swollen and altered connective-tissue fibrillæ. This change Neumann terms "fibrinoid degeneration" of the connective tissue. He admits that, in acute cases free from connective-tissue proliferation, the fibrin is more probably the result of exudation. Now it is quite true that there are cases in which one cannot say certainly what is the nature of the cells seen under the fibrin; yet there are other cases in which there cannot be a doubt as to their endothelial nature. As Lubarsch (67) points out, this can be proved experimentally by causing a minimal acute local peritonitis, by simply pulling out a loop of intestine, pinching it with sterile forceps, and replacing it. If the animal be killed, in thirty-six hours small spots may be found here and there, which are covered with a finely granular, scarcely visible deposit of fibrin; in such local deposits a continuous layer of endothelial cells can be made out passing well under the fibrin, which is pure exudate. Neumann's layer of endothelium covering the false membrane certainly exists in several cases, but it is clearly of secondary development. Gaylord (127), who made a full study of the subject under Orth, has shown clearly that after introducing fibrin or fibrin-forming fluids into the serous cavities, the endothelium proliferates and covers over this foreign fibrin, sometimes before any signs of organisation appear in the mass. Undoubtedly connective tissue undergoes a change in the inflammatory area; the bundles of fibrillæ swell, become more hyaline, lose their fibrillar appearance, and form more homogeneous glistening bands. But this modified connective tissue can generally be distinguished from fibrin proper if suitably stained by employing van Gieson's stain, or thionin.

The researches of Leo Loeb (128), conducted in my laboratory, possibly throw some light upon this subject. Taking a little lobsters' blood in which coagulation has been delayed by the addition of a solution of adrenalin chloride, and placing this upon a slide, then covering this with a second slide and pulling the one slide over the other so as to exert traction, it can be seen under the microscope that the cells, arranging themselves in rows, become transformed into a system of threads, and here and there the threads can be seen passing through a cell or even through the nucleus of a cell; the cells often become spindle-shaped and may either be so drawn out that their protoplasm forms long threads, or fine fibrillar threads may be seen actually passing through several cells. A similar transformation into fibrils can be produced by traction upon the protoplasm of exploded cells. It is worthy of note that, during either process, the cell-granules disappear, and these fibrillæ have staining and other reactions which connect them both with

fibrin and with connective tissue. Many of them, for example, stain well by Mallory's connective-tissue stain. In other words, these observations of Loeb favour the view that the conversion of the protoplasm of connective tissue cells into fibrillæ, is the result of tension and traction, *i.e.* of physical agents, and that the same is true also of the development of the threads of fibrin. If the same process be at work in both conditions, there is little wonder that it is difficult to draw a sharp line of distinction between the intra- and extra-cellular process in tissues where both are occurring at the same time.

Leaving out of account coagulation-necrosis as not occurring in direct connexion with exudates, it may be said that similar fibrin formation is frequently recognisable in connexion with primary inflammation of parenchymatous tissues.[1]

The beneficial effects of fibrin formation in serous cavities have been rendered abundantly manifest by the increase in abdominal surgery. No one who has followed any considerable number of operations for appendicitis can have failed to remark how, in case after case, despite the intricacy of the intestinal coils and their mobility, the strongly irritant matter produced by gangrene of the appendix, or oozing through perforations in it, is restricted within a relatively small space by the surrounding fibrinous adhesions which form rapidly between the intestinal loops. By this means alone the peritonitis is restricted and "regional," instead of being generalised from the onset. Even when inflammation (as in pericarditis) affects the whole extent of a serous cavity, the layer of fibrin acts as a protective coat closing the lymphatic "stomata," hindering the free absorption of the morbid material by the lymph- and blood-vessels, and filtering bacteria out of such fluid as does find its way through to the tissues beneath. It is not a little remarkable to call to mind how case after case of purulent pericarditis or purulent pleurisy may be examined in which, despite the intense suppurative disturbance in the serous cavity, the tissues at the other side of the deposit of fibrin—the myocardium or the lung tissue—show little or no tendency to abscess formation. Let there be primary abscess-formation or gangrene in the lung, and perforation of the pleura and pleurisy may supervene: generalised pleurisy, however intense, does not lead to this unless complicated by other disease. Let there be primary or metastatic abscess in the myocardium, then there may be aneurysm and rupture of the heart; yet such rupture produced by extension inwards of a purulent pericarditis is of the utmost rarity. Let there be inflammation originating in the submucosa of the intestines, as in enteric fever, and perforation may result; general peritonitis, while often due to perforation, never—so far as I can call to mind—directly induces that event.[2]

[1] Where there are abundant and distensible lymph-channels extensive clotting may be seen in the lymph. This is peculiarly well marked in the contagious pneumonia of cattle (contagious pleuro-pneumonia). In acute inflammation of various organs, by appropriate methods of staining, similar formations of threads of fibrin, often starting from cells as centres, may be observed in the tissue spaces.

[2] Where, however, there are localised pockets of pus such perforation may occur, and what I have termed "exogenous perforative ulceration" of the intestines is much commoner

In all these cases the natural protective layer of the serous surface is removed or gravely injured at a very early stage; and the layer of fibrin, replacing the serous endothelium, forms an effective barrier. I may add that the mucin, extruded so as to form a layer over inflamed mucous surfaces, presents a similar protective action.

But here again attention should be called to the fact that, while we can thus recognise an action beneficial to the economy in the laying down of fibrin, the adaptation to the needs of the economy is very far from being perfect, and the ultimate results are even replete with danger. I know of no better example than is to be derived from a study of the great omentum in a series of cases of abdominal disturbance (130). Time and again we find that this which, with the peristaltic action of the bowels appears to be in constant movement over their surface, has become attached by fibrinous adhesions over some inflamed area, thereby acting as a plaster or pad, reinforcing a weak point and, by the adhesions, preventing generalised peritoneal infection. From this aspect alone, the great omentum can only be likened to a brooding abdominal providence. But, when these adhesions organise, the omentum, now firmly attached, forms a band or bands of most dangerous import; now constricting a coil of the intestine and so causing obstruction, or kinking the bowel, or leading to internal hernia and volvulus. In short, the late results of adhesions may be very serious.

The fibrin so thrown out, while it may (1) be dissolved by the action of bacterial products, or (2) undergo complete absorption by the cells and fluids of the body with *restitutio ad integrum* of the affected areas, may also (3) form a frame-work upon which new tissue-growth occurs with replacement by organised connective tissue. This new tissue-formation in inflammation we shall discuss later.

Passing now to the ferments and ferment-like bodies present in the exudate, I may briefly state that these are not only generated and excreted by the pathogenetic bacteria present, but are liberated by the breaking down of the wandering cells. Abundant evidence of the existence of bacterial ferments capable of acting upon proteids, gelatine, sugars, etc., is supplied by the study of the growth of these microbes outside the body. No less than six such enzymes are said to be produced by the B. pyocyaneus, for it has been shown that dead cultures of this organism will liquefy gelatine, coagulate milk, and redissolve the coagulum, invert cane sugar, split up fats, and decompose proteids. That ferments also originate from the wandering cells has been demonstrated by Leber (29), who, placing pieces of copper in the anterior chamber of the eye, thereby produced a purulent collection devoid of microbes, and showed that the exudate was capable of digesting proteid matter. In this the leucocytes do not differ from the other cells comprising the organism.

than is generally suspected (129). Thus in 700 autopsies in all conditions, I encountered it seventeen times. The conditions favouring the development of the condition are adhesions after general or local peritonitis: formation of a pocket of pus, or abscess, between them; tension, acting with most effect on a soft walled viscus; compression, anæmia, and malnutrition of the wall; lessened vitality; infection; ulceration; perforation.

There have of late years been abundant observations by Salkowski (131), Jacoby (132), Conradi (133), and many others, upon the phenomena of autolysis, or the self-digestion of liver, muscle, and in fact most tissues, in which it has been shown that without bacterial action, possibly by the action of their own juices, the cells are able to digest and disintegrate themselves. Only in the inflammatory exudate the conditions favouring such self-digestion would seem to be markedly augmented. Müller (134) has shown that pus has a strong digestive action upon dead tissues, and to such autolytic action is now ascribed, on what appear to be convincing grounds, the resolution of the pneumonic exudate.

It would seem, therefore, that, more especially in pyogenetic inflammation, the removal of dead tissue cells and dead leucocytes may, to a large extent, be due to the action of the inflammatory exudations, apart from any phagocytic action on the part of living active cells; although this also comes often into play.

The bactericidal substances present in the inflammatory exudate have already been considered. We have abundant evidence that substances capable either of destroying microbes or of hindering their growth are present therein.

Summary.—To sum up what is known concerning the inflammatory exudate, it may be said—

1. That the exudate varies in amount and in character with (*a*) the nature and intensity of the irritant, (*b*) the condition of the organism, (*c*) the region of irritation.

2. That while it undoubtedly augments the nutrition of the affected region, increased nutrition at the early stage of an acute inflammatory process would not seem to be of benefit or to play any important part. At a later stage and in chronic inflammation the increased nutrition possibly aids the hyperplasia.

3. That in many cases the exudate exerts a beneficial action by flushing out the injured area. But this same flushing-out, by distributing the microbic irritants, may also be harmful to the economy.

4. That the exudate plays an important part in diluting the irritant.

5. That the development of fibrin in certain inflammatory exudates is associated with the breaking down of the wandering cells, and is of manifest benefit in so far as it circumscribes the inflamed area, and prevents the passage of morbid material outwards. Here again the action, by favouring the development of organised adhesions, may be deleterious.

6. That the exudate may possess digestive functions, causing the production of albumoses and other products of nitrogenous disintegration; the ferments being developed from the cells alone when the exudate is aseptic, from these and the microbes together when pathogenetic microbes are present.

7. That the exudate may further contain substances, generated by the cells, capable of hindering bacterial growth, and of destroying pathogenetic microbes.

III.—The Blood-Vessels

Chapter 16.—The Part played by Blood-Vessels

The study of the action and function of the leucocytes in inflammation has profoundly modified our conception of the inflammatory process. When the leucocytes were regarded as purely passive agents, and their diapedesis as purely secondary to modified conditions of the blood current and of the vascular walls, Cohnheim's hypothesis was that most generally accepted; this hypothesis regarded the changes in the vessels as of the first importance. Thus it was that for several years our attention was mainly concentrated upon the determination of the various changes of the vessel-walls, and of the mechanism whereby these changes were brought about. Nowadays less attention is directed to this side of the inflammatory process, and it may be said that during the last ten years little advance has been made in determining the mechanism of the dilatation that accompanies inflammation. The subject, indeed, is beset with difficulties. It is most difficult to observe the changes that occur in the cells forming the endothelium of the congested vessels; we are still, for instance, far from being sure whether the opinion of Arnold (135) is correct, namely, that the leucocytes, and, it may be, a large portion of the exuded plasma, find their way out through the dilated stomata between the endothelial cells; or whether the leucocytes pass directly through these cells as one soap bubble may be passed through another. And when we come to discuss whether the inflammatory exudation be a filtration, or whether, on the other hand, it be more of the nature of an excretion, or what may be termed a selective filtration—certain components of the blood-plasma being permitted to pass through, while others are withheld—we are met with the difficulty that, of the extravasated leucocytes, a varying proportion undergo rapid destruction and dissolution. Thus, in analysing the inflammatory serum, we are not dealing simply with the extravasated fluid, but with a fluid which in addition contains proteid and other constituents derived largely from broken-down white corpuscles, and in part, it may be, from the modified cells of the inflamed area.

Though Arnold's observations upon the altered condition of the vascular endothelium in inflammation appear at first very convincing, upon further study they seem at most to indicate that with dilatation of the vessels there is an increase in the size of the spaces between the endothelial cells. They do not, however, prove that these are other than virtual spaces filled with intercellular substance; and indeed Arnold himself came eventually to the conclusion that some such substance was present. That viscid, gelatinous substances injected into the circulation may be detected passing through these stigmata is not a proof that the spaces are actual; all it proves is that the walls are weaker in these regions; it must be remembered that increased force and increased

intravascular pressure are necessary to promote the passage of the injected mass along the vessels. The passage of the mass through the walls may therefore be an "artefact."

Kolossow (136) has demonstrated that the endothelial cells of the intima of vessels are not absolutely independent units, and that they are connected one with the other by numerous fine bridges or bridges of cytoplasm. Between these bridges are the stigmata; stomata—larger spaces—are not normally present between capillary endothelial cells. He holds that, normally, the cuticular portions of the cells are in apposition, but that with distension the stigmata from being potential become actual spaces, through which the migration of leucocytes and the escape of fluid may take place.

There is this further difficulty in the assumption that these are actual spaces—that in acute inflammation the exuded fluid contains a smaller quantity of proteids than does the blood-plasma. It is true, no doubt, that the stigmata are so small they may possibly act like the pores of a filter, and consequently may not permit the free passage of certain constituents of blood-plasma. To enter into the large subject of the nature of lymph would be to pass too far afield; I can here only say that taking into consideration the abundant evidence we possess of the activity of endothelial cells—influenced also, it may be, by loyalty to my old master Heidenhain—I have not become convinced by the brilliant researches of Prof. Starling that these cells have no selective activity, governing to some considerable extent the quality and the quantity of the exudate.

We have not a little evidence that these cells play an important part in the vascular phenomena of inflammation. To their power of taking up microbes and acting as phagocytes I have already referred; into their connexion with the slowing of the blood-stream I shall enter later. Here I would point out that microscopically these cells can be seen to alter during the inflammatory process; they become enlarged and project into the lumen of the smaller vessels, and in my experience this enlargement affects not only the cell-bodies, but also the nuclei, which at the same time would seem to contain more chromatin and to stain more intensely. In cases of chronic inflammation the enlargement is followed by proliferation, notably in the arterioles and capillaries,—a process which may lead to the ultimate occlusion of these small vessels. And in acute inflammation mitosis is to be seen occurring in these endothelial cells at an earlier period than in the surrounding tissues.

A further and very important process intimately connected with the proliferation of the endothelium of the capillaries is the formation of new vessels as the result of continued inflammation. It is true that Rindfleisch (137) and others have described this as being brought about by vaso-formative cells situated externally to the vessels; and that others have advanced so far as to suggest that there are cells in the newly-forming granulation-tissue which become hollowed out and gain attachment to the pre-existing capillaries in a manner wholly similar to that observable in the vascular zone of the embryo of the chick.

The search for the earliest signs of new capillaries is a matter of some difficulty. I will not peremptorily state that Rindfleisch mistook an arrangement of cells not unfrequently seen in granulation-tissue for stages in the development of new vessels. My own observations coincide with those of Arnold, Ziegler (138), and of the majority of those who have more recently studied the question, and lead me to regard the formation of new capillaries as originating from the endothelium of the vascular loops already in existence.

The first step in the process is often recognisable, in cases of pleurisy and pericarditis, in the projection of loops of pre-existing capillaries beyond the line which indicates where the serous endothelium used to be, and into the fibrinous clot now adherent to the sub-endothelial layer. Such loops are markedly distended, and "point," as it were, at right angles to the denuded surface. A similar pointing or giving way of the wall along the convex margin of the loop is also to be made out not unfrequently in newly-developed capillaries. In these there is not, as might be expected, a thinning of the endothelium along this outer margin, but certain of the cells on the contrary appear large and active. At times a small sharp protrusion of the vessel-wall can be detected in the region of pointing. This is best seen in the capillaries that are themselves but newly formed, and composed of nothing but a layer of young endothelial cells. In this layer the protrusion can be made out to be in direct continuity with the endothelial cells of the region. At first it is solid, but in the later stages it can be seen to be nucleated, and to be growing by proliferation of the endothelial cells which thus jut outwards. Even before any further change is noticeable in this projection from the capillary wall it may be seen to be united with a similar process originating from a neighbouring vascular loop. Finally, it would appear that the joined processes become hollowed out, and thus are developed into fully-formed capillary loops. It seems impossible to make precise observations on the phenomena of new vascular formation in its successive stages. I can but state that these appear to be the steps of the process. By what means the new vascular projections join together to form loops we are ignorant. Metchnikoff suggests that there must be an attraction between the neighbouring projections—a chemiotaxis—leading them to come into apposition; that chemiotaxis is a factor in the formation of new vessels has been indicated by Councilman (24), who has pointed out that where, in keratitis, the lesion is exactly central these new vessels are seen advancing inwards all around the periphery; where the lesion is eccentric these form only on the side nearest the lesion. That they do join is very clear to those who have studied granulation-tissue, or have observed the vascular network connecting the previously separated surfaces of a wound.

A further function of the vessel-walls is to be seen in the slowing of the blood-current. It is difficult, and in fact impossible, to explain this slowing by altered diameter of the arteries and veins. The alterations observed in the diameters of the vessels of the inflamed area are such as,

acting alone, would lead to increased rate of flow. Nor again is the apparent amount of exudation, and of lymph-flow from the affected part, sufficient to make it probable that (as Wharton Jones (139) first suggested) the slowing is in the main due to the concentration of the

FIG. 79.—Formation of new vessels in inflammatory tissue. (1) From a Ziegler's chamber (*i.e.* one formed of two cover-slips) left in the peritoneal cavity for forty-eight days. The tissue formed between the cover-slips consists of uninucleated and multinucleated formative cells. It is bounded by fully-formed new capillaries, and in the angle between these the solid buds or processes of developing new capillaries are well seen. (2) Formative (connective tissue) cells in direct con-[illegible] with the endothelium of newly-formed capillaries. From a similar preparation. (ZIEGLER.)

blood, relative drying of the corpuscles, and consequent increase of friction: while this may be an adjuvant we must, I think, find some more potent factor. What this factor is was pointed out long ago by Lord Lister (140), who, in 1858, noticed that coincident with the slowing of the blood-stream, the corpuscles move sluggishly along the vessel-wall as though attracted by it. He essayed to prove this by

an experiment performed previously by Weber (141). He ligatured a frog's leg, then irritated a portion of the web by a little mustard, and found that, although the blood-current had ceased, there was nevertheless an accumulation of corpuscles in the vessels of the irritated area, the corpuscles gliding into the affected region and becoming adherent there. Ryneck (142) has shown that this accumulation is not due to increased adhesiveness of the red corpuscles, inasmuch as similar slowing and stasis may be induced if the blood of the frog's leg be replaced by milk and the web irritated. In this case there is a gradual slowing of the stream of milk and accumulation of the fatty globules in the inflamed area. If, on the other hand, the vascular endothelium be killed by the action of circulating metallic poisons, then he found that no stasis occurred. And in favour of these views of Lord Lister and Ryneck is the fact already noted, that in inflammation the endothelium of the vessel-walls becomes altered, the cells becoming enlarged. With this, as evidenced by the conduct of the white corpuscles, they become more adhesive, and this adhesiveness with the associated increased friction between the vascular walls and contents I regard as the first factor in bringing about the slowing of the blood-stream. Let the current once accelerated be rendered slower by this increased friction, then transudation may accentuate the accumulation of corpuscles.

Summary.—While there is very much yet to be learned concerning the part played by the blood-vessels in inflammation, and while our present knowledge of this branch of the subject can only be regarded as very imperfect, the following may, I think, safely be said to epitomise what is known at the present time:—

(1) That the vascular walls, and more especially the endothelial cells lining the capillaries, play an active and not a passive part in the inflamed area.

(2) These cells have the power of throwing out pseudopodia and of taking up non-motile bacteria.

(3) They are larger and more prominent during inflammation than they are under conditions of health.

(4) From them are developed the new vascular loops in cases of more chronic inflammation.

(5) They would seem to become more adhesive in inflammation, and by this, in the first place, to lead to the adhesion of the leucocytes and red corpuscles to their walls.

(6) Similarly they would seem to cause an increased resistance to the passage of the blood-current, and in this way tend to slow the rate of blood-flow.

(7) The slowing of the stream may further be aided by the passage through the walls of increased amounts of fluid from the blood.

(8) It is impossible by analysis of the inflammatory exudation to determine whether this be a mere filtrate or be the result of a selective activity of the endothelium. On the whole there appears to be a combination of the two processes.

Other properties of the blood-vessels in respect of inflammation will be better discussed in later sections in connexion with the discussions of the part played by the nerves, and of the formation of new tissue.

Chapter 17.—On the Passage of Corpuscles out of the Vessels

By his researches, Cohnheim (1867) forcibly attracted the attention of pathologists to the diapedesis[1] of leucocytes in inflammation — a process which had already been described years before by W. Addison (143) (1843) and Waller (144) (1846) in England; and yet earlier (though without grasp of the connexion between the diapedesis and inflammation) by Dutrochet (145) in France (1828). Cohnheim recognised the amœboid nature of the leucocytes, and saw that once outside the vessels they moved actively, but eventually he could not discover that their penetration of the vessel-walls was anything but passive, although twenty years previously Augustus Waller had clearly described the active nature of the process; and this failure on Cohnheim's part to recognise the true nature of diapedesis confirmed him yet more strongly in the view that the all-important factors in the inflammatory state were the changes in the vessel-walls, and, it may truly be said, arrested his advance towards a fuller comprehension of the subject.

It must be acknowledged that there is much which would seem to support this view of the passivity of the leucocytes. No one is prepared to attribute active movements to the red corpuscles, nevertheless in inflammation a certain number of these escape through the vessel-walls. In the inflammation affecting some organs, notably the lungs, the number effecting a passage is very considerable. If, then, the red corpuscles emerge passively, why should not the emergence of the white be passive also? Add to this the very important observations made by Cohnheim, that where the circulation is arrested by compression of the artery there diapedesis ceases. This, if invariably true, would seem to indicate that when once by changes in the vessel the leucocytes adhere to the wall, the further passage through that wall is due to the *vis a tergo* of the blood-pressure.

This, however, is not a safe deduction to draw from the experiment referred to. When the artery of an inflamed area is compressed the stoppage of the blood-stream not only reduces the pressure, but also affects the quality of the blood and the conditions of the vessel-walls; moreover, it must profoundly affect the vitality and activity of the contained leucocytes. These considerations alone render the experiment valueless as a proof of the passive nature of the diapedesis. Again the passage outwards of red corpuscles does not occur in the earliest stages

[1] It has been objected that the term "diapedesis" should strictly be employed to denote only the passive transit of red corpuscles out of the vessels. If the word was originally employed in this sense it was an incorrect use: the term clearly indicates an active process—a "footing through" or jumping through.

of reaction to irritation; it never precedes the diapedesis of the leucocytes (save where there is gross injury), but follows it. A capillary or small vein in the inflamed frog's web, for example, may be seen wholly filled with corpuscles, the peripheral zone being quite annihilated, and numerous red corpuscles lying in immediate contact with the walls; nevertheless at first leucocytes only emigrate. This difference must be due to some special property of these cells. The leucocytes in the blood-stream are not necessarily globular passive agents, but are capable of independent movement. Leber (29), in his long series of studies, has pointed out that if, with due precautions, a hooked glass tube (closed at its outer end where it catches into the incision in the wall) be inserted into a large vein no thrombosis may be set up around the intravascular portion, and yet, upon removal, a large collection of leucocytes may be found in the tube, attracted by a drop of mercury placed, along with normal salt solution, within it. (Mercury is a substance which within the tissues leads to an accumulation of leucocytes.) Here, then, there must be active attraction and active movement of the leucocytes within the blood-stream. And Lavdowsky (147) has described very exactly what other observers had also noted, namely, that in inflammation the leucocytes in the outer zone of the blood-stream do not simply adhere passively to the wall, but move backwards and forwards before they attach themselves and emigrate, as though seeking for a point of less resistance. At times this movement is in a direction opposite to that of the blood-current. Further, Councilman has called attention to the suggestive fact that in the process of migration the nucleus is always directed to the objective point and, with a small surrounding of cytoplasm, is the first part of the cell to pass through the capillary wall. More than one observer has seen a relationship between the labile, broken-up character of the nucleus of polymorphonuclear leucocytes and their function of passage through minute orifices in the capillary walls.

If both within and without the vessels the leucocytes can be actively amœboid, it is strange that they should be passive in the process of diapedesis which to the eye has so characteristically amœboid an appearance.

As above stated, the compression of the artery passing to an inflamed area is in most cases sufficient to arrest diapedesis in that area, and I have suggested that this arrest may be due to the altered environment of the leucocytes. Now, if an embryonic form be taken, in which the tissues would seem to possess greater inherent vitality coupled with less sensibility, the arrest does not necessarily occur. Thus, Metchnikoff has noted that diapedesis of the leucocytes can be followed in the tadpole's tail, after the animal has been curarised to such an extent that the heart has ceased to beat and the blood in the capillaries has been brought to a standstill.

It is evident, therefore, that with our present knowledge we must regard the diapedesis of the leucocytes as an active migration, and must look upon the blood-pressure, the disposition of the blood-stream, and the altered condition of the endothelium of the dilated vessels as adju-

vants in the process. The slowing of the blood-stream and the diminished pressure in the inflamed capillaries render it more easy for the leucocytes to accumulate close to the vessel-wall; the dilatation of the vessels and consequent thinning of the walls, with the opening, perhaps, of larger spaces of cement substance or stigmata between the individual endothelial cells, render it more easy for the leucocytes to accomplish the passage; but the movement from within the capillaries to the tissue-spaces outside is an active process due to amœboid movement of the leucocytes themselves. The continuity of the vessel-wall once destroyed, other cells—red corpuscles—may be pressed passively through the walls.

FIG. 80.—1. Capillary (inflamed) of frog seen in profile, exhibiting margination of leucocytes, assumption of pear-shaped form, and migration through wall; a leucocyte adherent by long process. 2. Leucocytes in process of diapedesis, showing the pseudopodia on the outer aspect of capillary. From mesentery of rabbit, also in profile: higher magnification. [LAVDOWSKY.]

If this view be accepted, we are bound to look beyond Cohnheim's limit of changes in the vessel-wall for the stimulus which, originating in the area of irritation, acts upon the vessel-wall and the leucocytes in contact with it, and, having first set up changes in the former, so reacts upon the latter that they emigrate; or, to put it in other words, are attracted out of the capillaries towards the focus of irritation. It has already been shown that the movement of wandering cells in the tissue is due to the attraction of a diffusible product of bacterial growth and of tissue change, and of sundry organic and inorganic materials — the force to which the name of positive chemiotaxis has been given. Chemiotaxis must be invoked to explain the active emigration of the leucocytes from the capillaries, and again to explain its cessation under other conditions. Thus, while the exposed mesentery of a frog is a tissue in which diapedesis can be observed with facility under ordinary conditions, if it be washed with a weak solution of quinine, the leucocytes in the vessels remain globular, cease to adhere to the walls, and do not emigrate. This observation, first noted by Binz (148), has been confirmed by others, among whom Disselhorst (149) made out also that, if these same leucocytes be removed from the vessels, they exhibit their usual amœboid

movements. The quinine has not paralysed them, as Binz supposed; but, as Metchnikoff pointed out, it has neutralised the previous positive attraction, a negative or repulsive chemiotaxis being brought into play. It is difficult to see how these observations can be otherwise explained.

The view that diapedesis is an active process gains further support from, and at the same time explains certain interesting observations made by Bouchard (150), Roger (151), Charrin (152), and Ruffer. These observers have independently shown that in sundry instances the results of local injection of virulent cultures are greatly modified if, shortly before or coincidently, the microbes and their products are introduced into the circulation. Thus, as Dr. Ruffer points out (153), a drop of the culture of the bacillus pyocyaneus inoculated into the anterior chamber of the rabbit's eye leads ordinarily to a great migration of leucocytes—to an acute purulent inflammation. If, however, the toxins produced by this microbe have previously been injected into the circulating blood, no accumulation of leucocytes follows inoculation into the eye. Dr. Ruffer also extended most suggestively certain observations of Roger (151). Subcutaneous or intramuscular inoculation of the rabbit with the bacillus of symptomatic anthrax leads to the production of a local abscess with extensive accumulation of leucocytes. After simultaneous injections of fluid containing virulent bacilli and their products into the vein of the ear and the muscles of the hind leg, Dr. Ruffer found the rabbit dead, within fifteen hours, with a huge tumour in the inoculated limb. Here, upon examination, the muscle-fibres were found widely separated by fluid exudate, in which there had been great multiplication of the bacilli; but leucocytes were entirely absent. In these two cases we have therefore diapedesis and determination of leucocytes following the purely local action of the toxin; want of diapedesis and absence of leucocytes when the toxin at the same time circulates in the blood-stream. Wholly in line with these are the observations of Sidler (154). Solution of iodine, injected subcutaneously into the ear of a rabbit, sets up an inflammation characterised by extensive exudation with associated abundant migration of leucocytes into the part. With the injection of 0·05 per cent iodine solution peripherally into the ear vein there is the same or even more extensive fluid exudate, but no leucocytosis. If any large proportion of the leucocytes which find their way to a focus of irritation emerge from the blood-stream, these divergent results are only to be explained by some hypothesis which is capable of reconciling the difference in the action of the leucocytes when they are circulating in normal and in toxin- or irritant-containing blood respectively.

Now, the results in these cases are entirely consonant with what we know concerning the sensitiveness and reaction to stimuli not only of unicellular organisms, but also of the higher animals. Organisms, whether lowly or of most complex development, only perceive and react to alteration in their environment when the alteration exceeds a definite

ratio. Thus, as Pfeiffer has pointed out, a motile bacterium (the "B. termo") is attracted towards solutions of peptone; if it be already in a peptone solution, in order for it to be attracted towards and move into a more concentrated solution, this last must be five times as strong as is the former. This is in conformity with the psychophysical law of Weber-Fechner: that sensibility increases in arithmetical ratio when the stimulus or excitation increases in geometrical ratio—or, in other words, reaction is in proportion to the logarithm of the excitation. The only possible explanation that I can see of the above observations of Dr. Ruffer, Roger, and Sidler is that the passage and want of passage of the leucocytes out of the vessels depends upon the ratio of diffusible bacterial products present in the blood-stream and in the tissues respectively. Where the products are localised at one focus in the tissues, the leucocytes are attracted out of the unaltered blood, and there is active diapedesis; where there was already a solution of the bacterial products in the blood, the ratio of difference between the percentage amount of toxin in blood and tissue may be insufficient to stimulate the leucocytes; no diapedesis then ensues.

As is well shown in the experiment with symptomatic anthrax, the presence of the bacillus and its products in the circulating blood did not prevent inflammation at the region of local injection; inflammation and exudation were abundantly manifest—there was, in fact, a more extensive exudation than ever. The irritant—that is to say, the toxic products of the bacilli—at the point of injection was in no wise hindered from exerting effects upon the fixed cells of the vessel-walls, and promoting all the changes in calibre and condition of the walls and in the blood-stream characteristic of inflammation. But with vascular changes, if anything more prominent than in the case where local inoculation alone had been practised, the leucocytes stayed within the vessels. Now the only cause to which we can attribute this abstention of the cells from emigration is lack of attraction—certainly not lack of vascular change or lack of blood-pressure.

Summary.—We are thus led to the following conclusions regarding the passage of cells out of the blood-stream into an inflamed area:—

1. The diapedesis of the leucocytes is, as the name implies, an active and not a passive process; it is due to active amœboid movements on the part of the cells.

2. The stimulus leading to diapedesis is that of positive chemiotaxis. It is the attraction exerted upon the leucocytes by the diffusible substances associated with the irritant.

3. Irritants, if themselves diffusible, or the diffusive substances developed while the irritants are within the tissues, are capable of two separate actions: one direct upon the vessel-walls, leading to vascular changes; the other through the walls upon the leucocytes, whereby emigration may be induced.

4. These two actions need not (and frequently do not) manifest themselves *pari passu*.

5. In relation to diapedesis, the dilatation of the vessels, the altered rate of blood-stream, the altered disposal of the corpuscles in the stream, and the modified endothelium, may all be regarded as adjuvants.

6. The passage of red blood corpuscles from the blood-vessels into the inflamed area is passive, due to the blood-pressure and to lack of continuity of the vessel-walls. Such lack of continuity is favoured in many instances by the migration of the leucocytes through the walls.

IV.—The Nervous System

Chapter 18.—On the Part played by the Nervous System

If the vascular changes in inflammation were due to reflex influences proceeding from the central nervous system, and were in fact controlled by the centres in the brain and spinal cord (as has been held by the supporters of neuro-humoral hypotheses), then, in the first place, there should be a rapid and almost immediate response on the part of the vessels of any region on the introduction of an irritant. But this is not by any means constantly observed. Thus, as Cohnheim pointed out, if croton oil be rubbed upon a rabbit's ear more than an hour may elapse before the first beginnings of hyperæmia can be detected; yet the inflammation eventually set up may be very intense. In the second place, section of all the nerves passing to any region of the body should have this effect, that injury in the region in question should be unaccompanied by the ordinary vascular reaction. But this is not the case. Divide all the nerves which supply a rabbit's ear, for example, and then injure that ear, either by heat, cold, or inoculation of pathogenetic micro-organisms, and inflammation manifests itself with all the stages recognisable in an ear with intact nerve-supply. The vascular changes which accompany inflammation can occur then independently of any central nervous influences.

We can proceed farther, and state that regions deprived of their nerve-supply are peculiarly prone to inflammatory changes. But this liability to inflammatory disturbances in such regions is not directly due to the destruction of vasomotor tracts and the cutting off of central influences from the vessels of the part, but is, it would seem, immediately connected with the loss of sensation. Divide the ocular branch of the fifth nerve of a rabbit, and, if the eye be not protected, ulceration and necrosis of the cornea manifest themselves in the course of a few days. Protect the eye, either by bringing the lids together or by placing a shade over it in such a way that dust and foreign particles are prevented from settling upon the surface, and no such ulcerative disturbance manifests itself. From this it is clear that the primary cause of the inflammation is not any trophic change in the region, but is the lack of sensation, whereby irritant substances are permitted to gain a lodgment upon the outer surface without any attempt being made to remove them.

That, in addition, there is a lowered vitality in parts deprived of their nerve-supply, and that this renders those parts a more favourable seat for inflammatory disturbances is more than probable; nevertheless, this would not seem to be the primary cause of the increased liability to inflammation (*vide* p. 553).

This, then, in the first place, is clearly recognisable—that the vascular changes accompanying inflammation can occur independently of central nervous influences. Hence it follows that there must be a *peripheral* nervous mechanism controlling the vessels. It remains, therefore, to determine the nature of this peripheral mechanism: is it wholly under the guidance of peripheral nerve-cells situated in the vessel walls, or is it, in part at least, idiocellular? In the present state of our knowledge the answer to this question must be guarded. The more carefully the innervation of the various regions is studied, the more clearly is it demonstrated that throughout all the tissues of the body there exists a wonderfully fine and complicated network of nerve-filaments with occasional isolated ganglion-cells. Yet proof is wanting that this system in connexion with the vessels is sensorimotor. Indeed, so far as regards the heart and ventricular muscle (which may be looked upon as the region of the vascular system wherein the motile portion of the walls has become specially developed), the researches of Romberg and His lead rather to the conclusion that the peripheral nervous system subserves sensation alone. Nevertheless, there are observations to the contrary. Mall (155), for instance, has demonstrated the existence of motor nerves in the portal vein, finding that after ligature of the thoracic aorta stimulation of the splanchnics causes the portal vein to contract until the lumen almost disappears. The portal vein, it is true, has functions differing from those of most other veins; but this observation renders it possible that some veins, at least, may be modified by central stimuli in the course of the inflammatory process.

At the same time, the more the activity of the various tissues is studied, the more fully it is seen that many cells retain what may be termed reminiscences of an earlier and more embryonic condition in which their functions were varied and less specialised. There is an inherent probability that the endothelial cells can react directly to stimuli, and that they are capable of idiopathic contraction and expansion on appropriate stimuli. We have seen that these cells are capable of taking up microbes, and thus seem to exhibit an independent activity similar to that observed in the amœba or the wandering phagocyte. If these cells, then, are capable of throwing out pseudopodia, and thus of enclosing non-motile bacteria, are they not capable of contracting and expanding, as a whole, according to the stimulus of altered environment? As a matter of fact, such contractility of the endothelial walls of the capillaries has been demonstrated by Klebs (156) and Severini (157). I cannot but conclude, then, that at least the endothelium of the capillaries is to some extent self-regulative or neuro-muscular. It is quite possible that the muscular coats of the smaller arteries are likewise capable of self-regula-

tion, and respond directly to stimuli. In their recent studies on the sympathetic innervation of the rabbit's ear Dr. and Miss Meltzer (162) have demonstrated that after section of all the sympathetic fibres to the ear, the resultant hyperæmia disappears in some days, the vessels contracting, and this before any signs of nerve-regeneration can be detected. In other words, the arteries regain their tenacity without the aid of extrinsic nervous influence. That inflammatory dilatation of the vessels differs from simple vasomotor dilatation they demonstrate by the action of adrenalin: this is followed by rapid contraction in the latter condition, but is without effect in the former. The continuance of pulsation in the veins of the bat's wing when the nerves have been cut through, suggests either that the muscle of the walls has independent action or the existence of local ganglionic centres.

There is, indeed, something characteristic about the inflammatory dilatation of vessels—something not observed in other conditions—in active arterial hyperæmia or in venous obstruction. As Samuel (116) points out, if intense venous obstruction of the rabbit's ear be produced, the larger vessels are seen greatly engorged; but puncture of the skin outside the visible vessels, or even of the ear with a fine needle in such a position, is not followed by the escape of even a drop of blood—the capillaries remaining contracted. Puncture outside the visible vessels in the inflamed ear and the outpouring of blood is quite extensive. There is, in short, an active dilatation of the capillaries.

This view—that the vascular phenomena of inflammation can occur independently of the central nervous system and of the peripheral nerves —does not imply that the nervous system, central and peripheral, is without its influence upon the process; far from it. We have evidence, in the first place, that the state of the vascular walls is modified after destruction or severance of the nerves. I do not here refer only to the consequent alterations in calibre of the vessels, but also to the changes in other properties. Thus Gergens (158), and to a less extent Rütimeyer (159), noticed that after destruction of the spinal cord the blood-vessels of the frog permit a larger quantity of fluid, and even particles of granular colouring matter, to permeate them.

In the second place, we have evidence that the central nervous system exercises some direct influence upon the inflammatory process. From Cohnheim onwards it has been a matter of common observation that when all the nerves of a part have been severed, the stages of the process succeed each other with greater rapidity. It may be that the modified state of the capillary walls, noted in the preceding paragraph, is capable of accounting for this fact, and that, in the absence of central influences, dilatation of the vessels and exudation of fluid lead to the cardinal symptoms of redness and swelling, with associated changes in the tissue, at an earlier period.

Of the part played by the different sets of nerves the external ear of the rabbit again furnishes an excellent study. This part has a double nerve-supply through the auriculars (major and minor) from the cervical

plexus and the sympathetic branches from the superior cervical ganglion: stimulation of the former leads to dilatation of the ear vessels, of the latter to contraction of the same. If, as shown by Samuel (160), the sympathetics be divided on the one side, and the auricular branches upon the other, the ear vessels of the former side become widely dilated, and those of the latter markedly constricted. Under these conditions, if both ears be subjected to the action of water warmed to 54° C. there is a characteristic difference in their reaction. In the organ deprived of sympathetic influence the congestion and hyperæmia become yet more pronounced: an acute inflammation sets in which proceeds rapidly to recovery. In the opposite ear, with its constricted vessels, no hyperæmia is set up; but there is stasis, and gangrene may supervene. These results have been confirmed by Roger (161), who, taking a rabbit and dividing the sympathetic on one side, and then inoculating both ears with like quantities of a culture of the streptococcus of erysipelas, found that the erysipelatous process manifested itself much more promptly upon the paralysed side, and came to an end at an earlier date. The reverse was the case when the auriculars of the one side had been divided: here the process was of slower development than on the intact side, and of slower course, resulting in mutilation of the organ. Further confirmation is afforded by the researches of Meltzer and Meltzer (162).

The inference to be drawn from these observations is that section of all the nerves passing to the rabbit's ear permits the inflammatory process to run a more rapid course; section of the sympathetics (vaso-constrictors) alone has the same effect; while the uncontrolled action of the sympathetics after section of the auriculars (vaso-dilators) hinders or prevents the manifestation of the ordinary processes of inflammation, and by preventing the destruction or removal of irritant matter favours necrosis of the tissues. We have yet to learn whether these results are capable of a general application, and to discover how far they are borne out by clinical observations on diverse cases of localised paralysis. So far as they go they afford direct evidence of the power of the central nervous system to modify the course of the inflammatory process, while they demonstrate admirably how potent an auxiliary is the dilatation of the vessels in the inflammatory process.

Other evidence that the state of the nerve-supply of a region influences the manifestation of inflammation is afforded in sundry neuropathies. In all of these, in the present state of our knowledge, it is difficult to trace out the nervous factors associated with the lesions to which I refer. Our knowledge of the respective influences of trophic and vasomotor nerves is far too limited to permit us to say more than that a relation exists between the condition of the nerve-supply of the affected area and the inflammatory lesions there observable; that in a certain number of cases inflammation affecting the area supplied by one branch of a nerve may have associated with it definite inflammatory disturbances in the areas supplied by other branches of the same nerve, and that, similarly, when inflammation affects a viscus, inflammatory phenomena may be

sympathetically developed in regions innervated from the same area in the brain or spinal cord. I have already given examples in support of the first statement: the familiar redness, swelling, heat, and pain of the side of the face which may accompany toothache is an example in support of the second. Drs. Head and Campbell's thorough studies upon Herpes zoster (162) show that lesions affecting the nerve centres—in this case the posterior root-ganglia—may be the main factor in the development of an intense inflammatory process in the areas governed by those centres—a process so far unassociated with the presence of bacteria, although the appearances suggest infection. Another example is to be found in the acute nephritis which at times rapidly follows the passage of a catheter or the impaction of a stone in the urethra. It is not unlikely that many of these sympathetic inflammations are not direct, but secondary. Thus, the first noticeable symptom of catheter fever is suppression of the urine. Such suppression might be brought about either by reflex contraction of the renal arteries, or, contrariwise, by reflex great dilatation and congestion of the vessels of the kidneys. If it be caused by the former then the nephritis can only be regarded as secondary, and as due to the injury done to the organ by the stoppage of its blood-supply for some little time. Undoubtedly in many cases of catheter fever the nephritis is infective: in some the condition supervenes so rapidly that it is difficult to believe that we have to deal with an ascending infection. Where there is infection it develops in such a way that we are led to see that the altered condition of the organ under various influences has favoured the inflammatory process.

From the multitude of the factors involved, these examples, taken separately, afford at most only a great probability that the nervous system can directly originate inflammatory changes. There is, however, the clearest proof that the nervous system does possess this power, and this is afforded by the results of certain observations upon hypnotic effects. In some persons susceptible to hypnotic suggestion, the suggestion that a red-hot substance has been placed upon the hand will, in the course of a few minutes, lead to great reddening of the part supposed to have been burned, and this reddening may be followed by great local exudation and swelling—in fact, by all the symptoms of acute inflammation, save this, that the exudation is simply serous, not passing on to anything approaching pus formation, *i.e.* the migration of leucocytes would seem to be wanting. Here then actual inflammatory reaction follows supposed injury.

It is unnecessary to do more than point out the light that this intervention of the central nervous system throws upon the subject of counter-irritation, and upon the modifications of the course of inflammations brought about by idiosyncrasy of the individual.

From what has been said in the preceding paragraphs it follows that:—

1. Acute inflammation in all its stages may proceed regularly in the absence of all centrifugal nervous influences.

2. The vessels of an injured area are capable of reacting apart from central influences; it may be either directly, or under the control of a peripheral system of nerve-cells.

3. The central nervous system is capable of modifying the process of inflammation. It would appear that when the vaso-dilators alone are called into action the successive stages of the process are accelerated. When the vaso-constrictors alone are acting the process is retarded.

4. Centrifugal impulses alone, apart from any local injury, may originate a succession of phenomena of inflammation in a part.

5. Hence, in all probability, a nervous and central origin must be ascribed to some, at least, of the sympathetic inflammations seen to occur in areas supplied by the other branches of a nerve supplying a part primarily inflamed; and again in areas supplied from the same region of the brain or cord as the inflamed organ.

V.—The Cells of the Tissues

As a consequence of irritation two opposed processes may be manifested in the cells of the affected area,—changes leading to impairment and death, and changes leading to overgrowth and proliferation; degeneration and regeneration.

Either of these two processes may, it is true, be wholly wanting. In very acute suppurative disturbances, destruction of the tissue-cells and the steps leading to destruction may be the only recognisable changes. Again, in the first stage of most injuries, whether of mechanical, chemical, or bacterial nature, degenerative changes are wont to take the lead. On the other hand, there are irritants so mild that little or no cell-destruction results from their action; an extreme example of this category of inflammations is seen in those epithelial overgrowths commonly known as "corns," due, as Sir James Paget pointed out in his lectures, to intermittent pressure and irritation of moderate intensity.[1] Other examples are to be found in the "catarrhal" inflammations, in which there is marked initial overgrowth and proliferation of the cells of mucous membranes; and in tuberculosis, again, in which characteristically the earliest effects upon the pre-existing cells, produced by the presence and growth of the tubercle bacilli, are those of enlargement and multiplication—necrotic changes, as a rule, only appearing at a much later stage.

[1] It may very well be that this is not an extreme example. Neoplasms as a class, whether malignant or benign, not improbably develop as a consequence of some irritation having an intensity just sufficient to induce cell-proliferation, and continued for a time sufficiently long to impress upon the cells of the affected tissues the habit of rapid multiplication. There is evidence both in animal and vegetable pathology favouring this relationship between inflammation and neoplastic growth. The objection may be raised, with considerable force, that substances which lead to cell-proliferation are stimuli and not irritants, and that a line should be drawn between inflammation proper and overgrowth the result of irritation. I, for one, would willingly make this difference, but while it is easy to draw the line in certain well-marked examples, in others, as I shall proceed to show, cellular proliferation is so essential a part of the whole inflammatory process that the division becomes impossible.

Once more, in the later healing stages of injuries, cell-proliferation may be in the field alone. Nevertheless, in a very great number, if not in the majority, of inflammations, the two processes may be found occurring together—destruction and degeneration being in evidence at the focus of irritation, and growth and proliferation towards the boundary zone, where the irritant is acting in a less concentrated form.

Although the two processes are thus so frequently associated, it will be well, for the orderly review of our subject, to consider them separately.

Chapter 19.—Degenerative Changes

Death of the pre-existing cells as an immediate consequence of injury cannot be regarded as one of the phenomena of the inflammatory process. Immediate death of the cells may be a result of injury, and the disintegration of the dead cells may in itself lead the way to all the symptoms of inflammation. But cessation of action is not reaction, nor is failure response, and throughout this article inflammation has been considered as the reaction following injury, and the response to it. Thus immediate death of tissue-cells is resultant and not reactive, and may be eliminated from the category of the essential phenomena of inflammation.

The same is to some extent true of cell-degeneration, but not entirely. While it is impossible now to accept Virchow's view, that inflammation is essentially a process characterised by increased nutritive changes in the cells of the tissues (164), it remains most probable that in very many cases irritation induces increased, even if perverted, activity of certain orders of cells. The proliferation, swelling, and more or less rapid degeneration of these cells cannot be wholly ascribed to the toxic influence of the irritant, but must in part be regarded as a result of over-stimulation and overwork. This is most noticeable in connexion with catarrhal and parenchymatous inflammations. In parenchymatous nephritis, for example, such as that set up by cantharidin or infection, the cells especially affected are those whose functions are especially excretory: and their degeneration would appear to be intimately related to the performance of their functions. Such degeneration, preceded or accompanied, as it so frequently is, by excessive proliferation, may truly be regarded as reactive, and not as wholly and primarily destructive.

Of the degenerations which affect the tissue-cells (and often at the same time the leucocytes) in inflammation there are many varieties; in fact, according to the nature of the irritant, one, or other, or all the degenerations affecting the tissues in different pathological conditions may manifest themselves, save, perhaps, simple atrophy and pigmental degeneration (as apart from pigmental infiltration). Most commonly recognised are cloudy and fatty changes, but mucoid and hydropic changes are far more frequent than is generally noted. Even so specialised a change as amyloid degeneration has been observed occurring locally in chronic inflammations—as, for example, in gummas; while

in these same chronic lesions hyaline degeneration in the vessel-walls is very frequent.

There is a further form of degeneration met with in inflammatory disturbances which deserves more recognition than it has generally received. This is what may be termed reversionary metamorphosis. To speak of it as reversionary degeneration is, perhaps, a misnomer, although, if the irritation be continued, the modified cells undergo atrophy and destruction. It is not seen in acute inflammations, but in more chronic cases. As I have pointed out elsewhere, functional activity and active growth and multiplication of the cells of the organism are largely incompatible. The performance of function necessitates katabolism and breaking down; growth demands a building-up and increase of the cellular bioplasm. Thus, in the course of active cell-multiplication, the individual units lose, to a certain extent, the finely differential histological features associated with the performance of special function, and revert to a simpler, more embryonic type. All inflammatory new growth, when active, presents, indeed, a reversionary character, the cells assuming appearances resembling those seen in the process of fœtal development. Even in the simplest of all tissues, namely, white fibrous connective tissue, this is to be observed. But, in some instances, it is peculiarly well marked. Muscle-fibres, for example, are developed from sarcoblasts—large cells, without a sign of striation but with abundant cytoplasm, tending to become multinucleated. In subacute inflammations affecting a muscle, the striation disappears, the nuclei multiply, and, from the common multinucleated mass, there may be budded off or separated, isolated cells resembling hyaline leucocytes with abundant cytoplasm; resembling, in fact, the embryonic sarcoblasts. The embryonic liver shows no differentiation between liver-cells and bile-duct; both are developed from indifferent strands of cells. In the process of development those destined to be liver-cells enlarge, become polygonal, and gain abundant cytoplasm; those destined to become bile-ducts remain small, multiply, and become arranged as an epithelium. Now, in chronic interstitial hepatitis (portal cirrhosis) of the progressive type, we at times surely recognise at the outer border of the affected lobules that the liver-cells become smaller and smaller. Their nuclei also are small, and they have little surrounding cytoplasm; they form into little worm-like strands of cells isolated by the newly formed connective tissue; here and there such strands can be followed in direct continuity with the more normal liver-cells of the lobule. These are not true bile-ducts, as they are sometimes mistakenly called: the cells are irregularly arranged and do not form a true epithelium; they are more of a reversion to the indifferent stage.[1]

[1] While these appearances can be made out in progressive cirrhosis, it should be noted that, in cirrhotic livers showing reactive hypertrophy, another condition giving somewhat the same general appearance is to be detected, namely, active budding and new formation of liver parenchyma proceeding from the bile-ducts (165). This is a process of another order, one of ascent, not of descent.

All these degenerations are inevitably associated with disturbance of the functions of the affected cells, and lead to their death if the irritation which has induced them be continued. But death is not the final stage to be considered. The ultimate fate of the necrosed cells varies according to the situation of the inflamed area, the intensity of the irritation, and the specific character of the irritant. From a free surface the dead material may be freely cast off. In acute suppurative inflammations, whether superficial or deep, and, in general, wherever there is an abundant determination of leucocytes, there obtains a digestion and solution of the necrosed cells; and, as I have already pointed out, this is associated with the liberation of many ferments, the development of peptones, albumoses, fatty acids, and other bodies, and is brought about largely through the extracellular action of the leucocytes and processes of autolysis. When there is a large area of cell-destruction, with well-developed encystment and limitation of necrosis by granulation-tissue, the solution of the dead material and subsequent absorption may be incomplete, and a fatty debris left behind, which may eventually become infiltrated with lime salts (calcareous infiltration, in the production of which, as Klotz (166) has recently demonstrated, the conversion of fatty acids into soluble soaps plays an important part). In tuberculosis, despite the presence of many leucocytes in the immediate vicinity, the dead material of the centre of the tubercle undergoes very little absorption, but remains as an inspissated, cheesy, and, later, calcareous mass. In syphilis, on the other hand, in large gummas, while there is similar death of the central cells and absence of removal, fatty metamorphosis does not occur nearly to the same extent, nor is there the same tendency towards calcification.

Lastly, although very little is known about the subject, it must be pointed out that along with the tissue-cells the intercellular matrix undergoes modifications or degenerative changes during inflammation. Among these, in all probability, is to be classed an increase in the amount of intercellular mucin, a mucoid degeneration. The inflammatory exudate is in many cases rich in mucin, and although our knowledge of the changes in the matrix is scanty, the fact that the tissue-cells in general show little evidence of storage of mucoid or mucinogenous material, renders it probable that what mucin is formed is either excreted or elaborated between the cells. Connective-tissue fibrils, as part of the matrix, become swollen and fused into hyaline bands or masses, in which the individual fibrillæ are no longer distinguishable: in acute inflammation the next stage is the dissolution and disappearance of this collagenous matter. In chronic disturbances they are especially prone to hyaline change.

Chapter 20.—Regenerative Changes

In the lower animals, as we know, injury and actual removal even of a large portion of the body may be followed by the complete reproduction

of the lost part. In man, however, this reproduction of lost tissue is reduced to its lowest point; the higher the tissue the less, and the less perfect, the reproduction. Speaking generally, the tissues which show the greatest potentiality for reproduction are the least highly organised—those composed of similar units. The "connective tissue" —the lowest and most widely distributed—retains the largest powers of proliferation and hyperplasia.

In ordinary inflammation, hypertrophy and hyperplasia of the connective-tissue cells are absent at the focus of irritation. Here degeneration is predominant. It is in the peripheral zone, away from the maximum concentration of the irritant, that (as shown in case after case of Leber's long series of studies upon injury to the cornea), the connective-tissue cells show signs of enlargement and proliferation, that they become more swollen and prominent, send out large processes, and may exhibit signs of active mitosis. It may be urged that this peripheral change is not inflammatory, but associated; yet, as I have already hinted, the signs of cellular regeneration may manifest themselves at so early a stage that it is impossible to disconnect them from the process of inflammation. This has been brought out with emphasis in Ranvier's interesting series of studies on irritation of the peritoneum by weak solutions of caustic substances, to which reference has already been made (p. 730). With abundant fibrinous exudate, engorgement of the vessels of the serous coat, presence of polymorphonuclear cells, and other signs of active inflammation, there is active, direct, followed by mitotic division of the endothelial cells, some of which become enormous—100 μ and more in diameter. These cells send out processes, and take, some of them, an active part in the formation of adhesions. This is agreed, though the exact part is still a matter of controversy, whether (von Brunn (50)) they merely afford the endothelial layer covering the newly organised adhesions, or actually in part develop into fibroblasts. Here the main point is that during active inflammation cells of endothelial type are often to be seen in a state of active enlargement and multiplication.

As Baumgarten (167) showed in his studies upon the development of tubercles, in the irritation set up by the growth of the B. tuberculosis in the tissue, a like overgrowth with proliferation of the fixed cells occurs in the immediate neighbourhood of the bacilli without any primary evidence of cell-degeneration. It is true that the researches of Borrel (74) have thrown doubt upon Baumgarten's observations, but they confirm the earlier researches so far as regards the mitosis of pre-existing cells, and the absence of degeneration of these in the earlier stages of the tuberculous growth. Borrel would regard all the large epithelioid cells of the tubercle as modified leucocytes. If we assume, as I think we must, that cells of the hyaline mononuclear type have a common origin, whether passing to the part from the blood or developing from pre-existing cells of the part—that hyaline mononuclear cells are derived from endothelial cells in the main—we then harmonise, or find *a via media* between, these opposing views.

The difficulty of determining the origin of the growing cells in inflammation has formed the greatest trial of the pathologist throughout an entire generation, and yet longer; nor can we now assert without chance of dispute what cells are mainly concerned in the formation of new tissue. When we examine newly formed granulation-tissue we can distinguish cells of more than one type—(1) small round cells with polylobular and fragmented nuclei, (2) other cells containing oxyphil granules, (3) larger cells with a single nucleus and a relatively large quantity of protoplasm, and again (4) cells of varying but generally large size, varying in shape, but on the whole having the appearance of spindle-cells with single oval nucleus and abundant protoplasm. These can be made out easily.

The first two forms of cells are clearly hæmatogenous leucocytes. Further study of their fate shows that they disappear; they play no

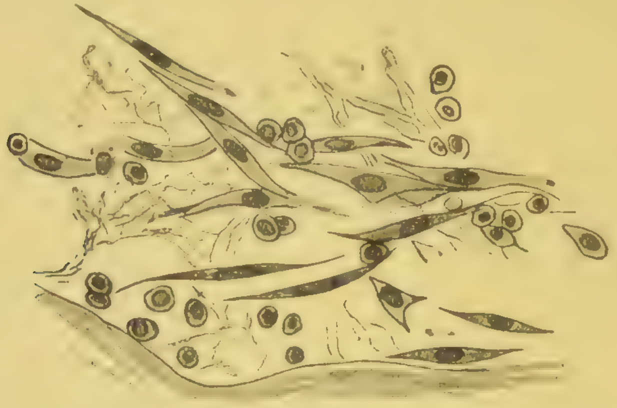

FIG. 81.—Spindle-cells and developing connective tissue in an air-sac of a piece of hardened lung introduced into the peritoneal cavity of a guinea-pig, showing well early stages of development of the fibroblast (seventh day). The cells lie in a network of fibrin. [MARCHAND.]

further part in the organisation of the tissue save that, as is well shown by Scheltema (168) and Nikiforoff (169), many of them are absorbed by the growing connective-tissue cells, and thus would seem to aid in their nutrition. The last form likewise presents, as such, no difficulties. These are fibroblasts—cells in the process of growth into connective tissue. But what is their relationship to the previous form,—to the round mononucleated cells with fairly abundant protoplasm,—what are these last, and what, in short, is the origin of the fibroblasts,—is it from leucocytes or from pre-existing connective-tissue cells? Upon this most difficult question more ingenuity and more research have been expended than upon any other part of this well-worked field of inflammation.

There can be no doubt now that a large proportion of the fibroblasts in granulation-tissue are developed from pre-existing connective-tissue cells. The general consensus of recent researches leads decidedly in this direction; and it is from the laboratory of Ziegler, who by his classical observations led pathologists for some years to hold the contrary view,

that the studies have emanated which most conclusively show the part played by the connective tissue; the researches of Krafft (170), Podwyssozki (171), Coen (172), Fischer (173), and Nikiforoff, confirmed and strengthened by the researches of Arnold (174), Marchand (175), Reinke (176), and Prof. Sherrington and Mr. Ballance (177), and the more recent researches of von Brunn, Maximow, Mönckeberg, and a host of other workers, all bring forward evidence in one direction. It is the clearly recognisable pre-existing cells of the tissue—connective, endothelial, and epithelial—which show most constantly the signs of nuclear division: every stage of enlargement, mitosis, and cell-division can be made out in them. Even if we did not possess the information afforded by nuclear changes, the fact that new tissue is always developed in the immediate neighbourhood of pre-existing tissue would in itself point strongly to this same conclusion.

We may rest assured of this much. But can we advance farther, and state that all newly formed connective-tissue cells originate from the pre-existing cells of the tissue, and that none of them are derived from wandering cells? In the present state of our knowledge the answer to this question must be an unhesitating "No." We have evidence, in the first place, that cells of the hyaline mononuclear type show all transitions from round- or spindle-shaped cells to definite fibroblasts in the process of forming connective-tissue fibrillæ (Maximow and others). Metchnikoff has followed day by day the transition from the interstitial wandering cell of this type into the connective-tissue cell; this in the tadpole's tail. Evidence was brought forward (*vide* p. 730 *et seq.*) that these hyaline mononuclear cells are histogenous, developed from pre-existing tissue, more particularly from connective-tissue endothelium. The proliferated and "embryonic" endothelial cells of vessels have been observed in the process of migration into the surrounding area; in short, proliferating tissue-cells in an area of inflammation, in the process of forming new cells, revert to a simpler, more embryonic type; they become round cells of the order of leucocytes; they exhibit phagocytic properties; they give off pseudopodia; they are capable of movement and translation; they become, for the time, wandering cells. And other cells of the same order, the hæmatogenous mononuclear leucocytes, which, as has been pointed out, are presumably of like endothelial—*i.e.* connective-tissue—origin, when they migrate into an area of inflammation have like properties. There are, in short, histogenous wandering cells, and, once this is admitted, active controversy, save on matters of detail, comes to an end. It may be stated that the fate of these histogenous wandering cells is a matter of environment, of relative position; if they remain in the neighbourhood of the vessels of the inflammatory zone, they are able to develop into fibroblasts, and give origin to new tissue; if, being of endothelial origin, they find themselves lying over a surface they form endothelium; if they wander further afield into the area of inflammatory necrosis they continue to comport themselves as wandering cells, at most acting as phagocytes, and undergoing eventual dissolution, or, more rarely, finding their way back

into the vascular system. Thus it is that, as already stated, new tissue is laid down always in the immediate neighbourhood of pre-existing tissue; that is to say, in the neighbourhood of blood-vessels and of adequate nutrition.

This, I believe, expresses the outcome of the more recent studies upon the matter, and to epitomise we may say :—

(1) Two series of changes may occur in the cells of an inflamed tissue, which may be included under the terms degeneration and regeneration respectively.

(2) The extent to which one or other of these series of changes predominates varies with the nature and intensity of the irritant.

(3) Degeneration and death of the tissue-cells may be a direct and immediate result of the presence of the irritant, and then can scarcely be regarded as essential phenomena of inflammation. Or they may be of more gradual onset, associated with evidence of over-stimulation and increased activity of the cells.

(4) Fatty, cloudy, hydropic, and mucoid are the most frequent forms of degeneration affecting the tissue-cells in acute inflammation; hyaline in chronic; other forms are rare.

(5) The ultimate fate of the necrosed cells varies as the situation, intensity of irritant, and specific character of the irritant.

(6) Cell-proliferation is so constant an accompaniment of certain forms of inflammation that it is impossible to regard this as an adjunct and not as an essential part of the process.

(7) The tissues which show the greatest potentiality for reproduction in consequence of inflammation are those which are least highly organised.

(8) The origin of fibroblasts and new connective-tissue cells is still in some details a matter of controversy, but this much would seem to be clearly demonstrated: That while the larger proportion of the fibroblasts are derived from the pre-existing connective-tissue cells of the part, others may have originated from histogenous wandering cells that have migrated from some distance. Free hæmatogenous leucocytes (polymorphonuclear and eosinphil) do not give rise to new tissue; whether lymphocytes can do so is still under debate. The practical identity between young cells of hyaline mononuclear type and newly proliferated connective-tissue and endothelial cells makes it impossible to determine with precision the point of origin of any individual cell by histological methods alone.

Chapter 21.—On Fibrous Hyperplasia and its Relationship to Inflammation

The succession of changes from embryonic cells to fully formed tissue can best be studied in cases where there has been a relatively large area of destruction—as, for example, after severe burns, or excision of organs or large portions of organs; or, again, where inflammation has been of a chronic character.

Granulation-tissue can be studied well in the granulating wound, a form of inflammation regarding which, as yet, we have said very little, frequent though it is in surgical experience. When, through injury, the skin or superficial protective layer of a part is removed or destroyed, and the underlying tissue exposed, the first stages are those already described, namely, of dilatation of the vessels in the immediate neighbourhood of the injury, exudation of fluid, migration of eucocytes, and so forth. The extent of the migration depends largely upon whether the wound has become infected or no; but even where infection from without has been prevented, in every case where deeper layers are exposed, and not brought together, there is a certain amount of diapedesis, apparently induced by the presence of products of cell- and tissue-destruction. Where superficial infection takes place, the migration of leucocytes is much more abundant, and in place of a thin layer of exudate tending to undergo coagulation and form a scab, there is a surface accumulation of pus, without coagulation. With the present aseptic methods of treating wounds we are not accustomed to see now any abundant development of pus over an exposed wound. Formerly it was different, and a distinction was made between laudable and foul pus; the former being bland, creamy, and of sweetish odour: the latter discoloured and foul through the abundance of putrefactive microbes, and accompanied by progressive breaking down of the tissue bordering on the wound. "Laudable pus" seems to us to-day a misnomer. With modern methods pus is regarded as matter out of place and far from praiseworthy. And yet more than one recent observer has shown, by direct experiment, that pus of this nature on an exposed surface has properties which we cannot describe as other than laudable. It has been shown to act as a barrier. Add to such pus covering a granulating wound a suspension of some known pathogenetic microbe, and, unless these be added in excess, they do not set up general infection; they are not to be detected in the underlying tissue. Pus is definitely bactericidal. It would seem that the underlying, newly formed granulation-tissue partakes also in these bactericidal properties (Jürgenlünas (178)).

For beneath this surface layer new tissue begins to form. The process of growth is seen to originate in the immediate neighbourhood of, if not in direct connexion with, the layer of dilated capillaries immediately bordering upon the wound. As already described, these project outwards towards the exposed surface, and from them are developed or projected new capillary loops. As these form there is a rather remarkable clearing in their immediate neighbourhood. The abundant leucocytes and fibrin (if present) or cell-debris disappear, and whether by phagocytosis, autolysis and dissolution, or by re-migration of the still active leucocytes into the vessels, the area immediately around the capillary loop becomes relatively free. From the first series of capillary loops other capillaries are projected, until the whole surface of the tissue, when cleansed, if necessary, of overlying pus, is seen to be covered with a finely granular or coarsely velvety, reddened, injected layer. This is granulation-tissue.

If healthy granulation-tissue be examined, the process of growth is

seen to originate in the immediate neighbourhood of, if not in direct connexion with, the dilated new capillaries. It is around these vessels, formed of little more than a single layer of cells, that the fusiform fibroblasts are in greatest abundance. At a later stage, in regions more remote from the advancing margin of the granulations, the fibroblasts have a more general distribution in the intercapillary spaces, and are more elongated; around them may be seen the earliest wavy fibres of white connective tissue. These are essentially of cellular origin—as much so as is the substance of striated muscle-fibres. The elongated fibroblasts not only break or extend at their poles into fine processes, but also along their sides the protoplasm undergoes modification into fine parallel fibrillæ. With the continuance of this change the cells become smaller and smaller until little is left but the attenuated nuclei, often so flattened and narrow as to be scarcely recognisable. With increasing age the fibrillar substance contracts; certainly the newly formed cicatricial tissue diminishes greatly in volume, and with this diminution the previous great vascularity of the part disappears; the capillaries shrink until the majority become completely occluded. Thus in place of the abundant, soft, and succulent granulation-tissue, rich in cells, blood-vessels, and exuded fluid, there is eventually a firm, shrunken, anæmic mass of fibrous tissue, with a few flattened nuclei, and rich only in closely pressed bundles of white, semi-transparent fibrils.

FIG. 82.—Granulation-tissue seen from the deeper toward the upper surface. 1. Spindle-cells, most abundant in deeper portions, where they are also becoming swollen; 2. Polymorphonuclear leucocytes, most abundant towards outer surface; 3. Lymphocytes; 4. Capillaries. (After RIBBERT.)

Elastic Tissue.—In the new tissue there may be a certain number of the coarse fibrils of elastic tissue. The development of these has been somewhat extensively studied of late. The conclusion reached is that their development is governed by cells which so far are not to be distinguished from those forming ordinary connective tissue (179).

Fibrosis.—Fibrous hyperplasia may be met with in almost every tissue of the body as a sequence of very diverse morbid conditions. To speak of it in any case as "fibroid degeneration" is a misnomer. The overgrowth of any tissue, however lowly, is not a degeneration. Fibrous tissue may and often does become the seat of degenerative processes, notably the hyaline; but that is another matter. To regard every condition of generalised or localised fibroid change of the organs of the body as a chronic "—itis" is equally erroneous; for, as we shall point out, there are conditions of fibrosis which cannot be regarded as the result of irritation and injury. And even when everything indicates that the fibroid change is of inflammatory origin, the caution must here be given that unless the condition is progressive, it is a source of confusion to term it a chronic "—itis." It is a mistake to term an old-standing case of complete pericardial adhesion "chronic pericarditis" unless there are indications that the condition is still advancing The inflammation may have been arrested years previously. Such a state should for clearness be spoken of as "pericardial adhesions" or "old adhesive pericarditis." It is interesting to note the opposed tendencies of the two branches of our profession on this subject; the surgeons strive to restrict the idea of inflammation to acute pyogenetic disturbance, the physicians to extend the idea so as to include all cases of chronic progressive "fibrosis." I will not say that the latter is as untenable a position as the former, for it is a matter of peculiar difficulty and delicacy to state what is and what is not an inflammatory fibrosis; after all, there is more danger of being tossed about helplessly in the Charybdis of including too little, than there is of striking upon the Scylla of including too much in our idea of inflammation.

Here I wish to point out how divergent are the conditions which lead to fibroid hyperplasia, and to show that there is reasonable ground for not classing all forms under the one common heading, even though the resulting appearances may be undistinguishable, and the effects the same.

Let us, in the first place, consider the conditions that are certainly of inflammatory origin. The study of the various stages in the development of a tubercle demonstrates that, in man and most mammals, the first result of the lodgment and growth of the tubercle bacillus in the tissues is to stimulate tissue-formation. Only at a later period, with continued action of the products of the bacillus, does tissue-destruction become manifest; and, even here, in a progressive tuberculosis of moderate intensity, we find that while in the central mass the new tissue is breaking down, at the periphery there is definite formation of new fibrous tissue. It cannot be said that here we have an instance of two processes, of inflammation and repair, going on simultaneously, for, studying a series of cases, we find that so-called repair—the tissue-overgrowth—precedes a so-called inflammatory disturbance—the necrosis and caseation; the same influence causes both conditions. This newly formed connective tissue is clearly a productive fibrosis of inflammatory origin.

Now let us consider what seems to be a very different condition.

Where there is atrophy or destruction of sundry motor centres in the brain or section of the lower part of the cord, or destructive lesions affecting the cells of the ganglia of the posterior nerve-roots, there results degeneration and death of the axons forming certain descending or ascending tracts in the cord; and the death of the axons is gradually followed by replacement with fibrous tissue. Here there has been no irritant from without circulating from the lymph-channels to the fibres and causing their destruction; the degeneration and the fibrosis have followed injury at a distance. Is this "replacement-fibrosis" to be regarded as a form of chronic inflammation? No exogenous irritant has been at work; nay, more, the process is so gradual that often none of the ordinary accompaniments of inflammation are to be recognised. Even in the early stages the indications of hyperæmia, migration of leucocytes, formation of new capillaries, are often of the slightest. But, on the other hand, what distinction is to be drawn between the process seen here and the grosser changes which occur in non-infective infarcts? Where, for instance, a branch of the renal artery becomes plugged by a mass of clot, and—as a consequence of the condition of the renal circulation—the area of kidney tissue served by this branch becomes wholly cut off from its blood-supply and dies, we find that the dead tissue becomes replaced by what is clearly cicatricial fibrous tissue. In such infarcts we can recognise the whole succession of inflammatory phenomena. The capillaries immediately surrounding the wedge of dead tissue become greatly dilated; there is abundant migration of leucocytes into the area; the dead tissues, by their action, become broken down and dissolved, and, coincidentally, the surrounding walls give off new capillary loops into the area. We have, in fact, the formation of granulation-tissue with a resultant fibrous tissue-formation and replacement of the dead by cicatricial tissue which, like cicatricial tissue in general, eventually contracts. Here surely we have an inflammatory process set up by the death of the kidney cells, which, dying, liberate diffusible irritants, initiating a series of changes in connexion with the surrounding vessels. The changes seen in the cord and in the kidney differ in degree only, not in kind.

We must thus recognise at least two types of inflammatory fibrous tissue-development; the one *productive* or *hyperplastic*; the other, as I have termed it, *replacement-fibrosis*. In the latter the amount of new fibrous tissue developed appears to be in proportion to the extent of the destructive process; in the former, continued irritation leads to an overgrowth not related to previous tissue-destruction.

Productive Fibroses.—Among these are to be included various localised fibroses, such as the focal areas of new connective-tissue growth set up by the presence of certain micro-organisms, notably those causing the more chronic types of infective granulomas, as, for example, the tuberculous nodules of the tubercle bacilli; syphilitic gummas; the nodules caused by the presence of leprosy bacilli; the extensive tumour-like masses set up in man and cattle by the ray fungus or actinomyces; the new growths around certain pathogenetic blastomycetes or yeasts, more particularly

studied by Gilchrist (180) and other American observers. Similar tubercle-like nodules may be formed around certain pathogenetic moulds (aspergilli) (Boyce (181) and others), and we encounter them also around minute larval nematode worms.

Not unlike these are the capsular fibroses, those cases of connective-tissue development forming around the irritant, whether infective or no. Here the zone of tissue-formation is a development of so much new material laid down irrespective of previous tissue-destruction ; the thick capsules forming around chronic abscesses and phthisical cavities ; around impacted bullets, or, as frequently observed in the lungs, around inhaled particles taken into the tissues by the agency of the leucocytes.

Here also must be included the fibrous overgrowth due to inflammation of serous surfaces, including in this the fibroid thickening of those surfaces and the development of organised inflammatory adhesions. The new formation in some of these cases may be most extensive, more particularly in conditions known as chronic hyperplastic serositis, or as Nicholls (182) has termed it, hyaloserositis ; the liver, spleen, or pleura may be covered by a thick layer of dense, hyaline, almost porcelain-like connective tissue laid down in successive layers which may be a centimetre or more in thickness.

With these are to be included the general productive fibroses of inflammatory origin affecting the substance of different organs. Such, for example, is the chronic interstitial pneumonia following upon chronic pleurisy, in which bands of fibrous tissue are laid down along the lymphatics passing from the pleural surface. And here also we may include the generalised interstitial fibrosis of so-called chronic parenchymatous diseases, such as we see, for example, in productive parenchymatous nephritis, in which, secondary to the inflammation of the tissue-cells proper of the organ, there is an overgrowth of the fibrous stroma. It is to be noted that some at least of these later cases must be regarded as admixtures of productive and replacement conditions, there being a coincident destruction of the parenchymatous cells.

Replacement-Fibroses.—Here we can distinguish certain well-defined types, though all may be termed cicatricial. Wherever we have breach of continuity in a part, there is a tendency for that breach to be filled up by new tissue. In some cases this new tissue is a regeneration of the higher specific cells of the injured organ. In general, however, it may be laid down that the more highly differentiated a tissue, the less is the capacity of its cells to regenerate, so that, more often, it is the lower, humbler connective tissue that repairs the breach. Under this heading, therefore, we place cicatrices of various orders, and include, as already stated, the replacement of *dead* tissue seen in a simple infarct, where there has been sudden death of the tissues (necrosis), and the replacement-fibrosis seen where tracts degenerate in the spinal cord, and other cases in which fibrosis follows necrobiosis, *i.e.* slower death of the tissue preceded by atrophy and degeneration. Possibly this is the right place also to include the organisation of thrombi ; that is to say, of masses of

coagulated blood within the vessels. When the blood thus coagulates, its cells largely break down, so that the fibrinous products may be regarded as non-living necrotic tissue. While this, in part, undergoes absorption, if it be not infected, a portion at least becomes organised by granulation-tissue, and so, eventually, is replaced by a fibroid mass.

We may thus classify the forms so far brought forward as follows :—

A. Productive or Hyperplastic Fibrosis :

- (1) Localised { focal, capsular.
- (2) Serous and adhesive { local, generalised.
- (3) Interstitial.

B. Replacement-Fibrosis .

- (1) Cicatricial.
- (2) Post-necrotic.
- (3) Post-atrophic.

C. Mixed Fibrosis : both processes being in evidence.

This does not, however, exhaust all the conditions of connective-tissue overgrowth occurring in the organs of the body. We have, in addition, fibroid neoplasia and fibromatosis. It is difficult in every case to separate these off sharply from the productive fibroses of inflammatory origin, for we have a series of what may be termed transitional forms. Typical, encapsulated, fibroid tumours develop without any clear history or indications of previous inflammation. We have here a neoplastic fibrosis or fibromatosis which, for the present at least, we must sharply distinguish from the inflammatory conditions, and that because, as already indicated, we are ignorant of its causation.

There is, however, a curious condition known as cheloid, especially liable to occur in certain races, as among negroes, and in certain families or individuals in which a very slight irritant, which in ordinary individuals would lead to no ill effects, is followed by a progressive growth of fibrous tissue. The pressure of a basket carried on the shoulder, or even of a collar button on the neck, has been known to set up this localised but subcutaneous-spreading fibrous overgrowth ; and, indeed, masses several pounds in weight have been so produced. In a case studied by one of my students, Mr. R. Martin (183), a mere scratch by a pin along the arm led to the appearance, in a few days, of a series of small new growths in the line of the scratch. Here, then, irritation originates a new growth that is wholly out of proportion to the intensity or duration of the irritation. This, however, is not a true fibromatosis, inasmuch as, frequently, the new growth undergoes atrophy and disappears. It is an intermediary condition between the two processes of inflammation and neoplasia.

As I have pointed out elsewhere, there is yet another series of cases in which what we may term stimulation rather than irritation—if we can draw a line between the two—is followed by new connective-tissue growth.

These cases I can but indicate here. I would only point out that in the ordinary form of arteriosclerosis, for example, fibroid thickening of the intima does not appear to be directly associated with inflammation of this portion of the artery; everything appears to indicate that it is the media that, undergoing degeneration, first gives way, and that the thickening of the intima and the overgrowth of its connective-tissue cells is wholly a compensatory process. I have suggested that, just as in those who are muscular and accustomed to active exertion, we find that the bone, subject to strain at the origin of the various tendons, shows there a marked over-development and growth into definite ridges, or even into processes, so, where the arterial wall gives way, the strain to which the well-nourished intimal cells are subjected favours their proliferation and the development, immediately beneath the endothelial surface, of layer upon layer of new cells, until—the area of dilatation being filled up by the new tissue—the calibre of the artery is restored to the normal, and the extra strain or tension upon the intimal cells is removed (184). As pointed out recently by my colleague, Dr. C. F. Martin (185), an allied fibrous overgrowth of the intima and media of veins is much more common than is usually imagined. Such *Phlebosclerosis* affects more particularly veins that are poorly supported, and this even in young adults; it is unassociated with any obvious signs of progressive inflammation, and must, Martin concludes, be placed in this group of "strain-fibroses." The overgrowth of fibrous tissue around the veins—in the liver, for example—in cases of prolonged chronic venous congestion (where this is not excessive),[1] and that remarkable connective-tissue overgrowth of a part in which there is obstruction to the main lymph-channels which constitutes the common type of elephantiasis, are both, we would suggest, of this same order of new connective-tissue growth, due rather to strain and stimulation than irritation, and so more of a physiological than of a pathological and inflammatory type.

In this connexion may be noted certain observations by Thoma (187). In his wonderfully painstaking series of observations upon arterial changes, he has adduced two cases which he describes as examples of "endarteritis," but in which the inflammation is not apparent, nor indeed any factor other than altered tension of the arterial walls leading to altered conditions of nutrition. He shows that immediately after birth there is developed a thickening of the intima—a connective-tissue proliferation immediately below the endothelium—of that portion of the aorta lying between the ductus Botali and the passing off of the umbilical arteries. During later fœtal life the umbilical arteries are the largest branches of the aorta; and, when the circulation through them is arrested, the aorta above is too large for the amount of blood requisite for the abdominal viscera and the lower extremities. The arterial current

[1] I agree with Dr. Rolleston (186) thus far, that advanced and severe passive congestion is not accompanied by fibrosis of the central veins of the liver lobules. I have, however, seen this well marked in cases where there has been a long-continued, slight grade of the condition.

becomes, therefore, relatively slowed, and presumably, judging by the analogy of what occurs in the adult when large branches of the aorta are ligatured, the aortic blood-pressure is for a time raised. With this slowing and increased pressure there appears a compensatory overgrowth of the intima leading to contraction of the vessel and its lumen. Generally speaking, when the area of distribution of an artery is diminished, as, for example, when a limb is amputated, the artery shows a similar proliferation of the intima. In both cases the blood remains healthy, and the intima has undergone no injury; the only recognisable change has been a slowing of the blood-stream, and probably increased blood-pressure; and as the intima is nourished, not through the vasa vasorum, but directly from the main arterial fluid, it would appear that with the slowing an increased nutrition is brought into action. This is Thoma's explanation: mine differs somewhat in regarding the overgrowth as resulting from increased strain coupled with increased nutrition. I can see no satisfactory reason for calling either of these cases an endarteritis. It is quite possible that other cases of thickening of the intima are due not to irritation, but to increased nutrition brought about by heightened arterial tension. The difficulty urged by Councilman (188), that high arterial pressure does not invariably lead to overgrowth of the intima, is not, in my opinion, insuperable. It must suffice if here I point out that it is more than probable that certain cases of endarteritis are in no sense of inflammatory origin, or secondary to degenerative changes; but are primarily associated with nutritional changes. In this connexion it was shown by the late Prof. Roy and myself (189) that when the aorta of the dog is suddenly and greatly constricted, and as a consequence the pressure in the proximal portion of the vessel greatly increased, the plasma of the blood is forced into the cusps of the aortic valves, and vesicles of lymph make their appearance on the under surface in that region where fibroid thickening is most frequent in cases of chronic high arterial pressure. And we are inclined to consider that some at least of the cases of chronic endocarditis, so-called—the cases in which there is a generalised diffuse thickening of the valve-segments with the non-vascular new fibrous tissue laid down in layers parallel to the surface, the most recent immediately beneath the endothelium—belong to this category of non-inflammatory fibroses.

Thus, to express briefly the distinction that we would draw between inflammatory and non-inflammatory fibrous hyperplasia, I would say that where *local injury* leads to increased nutrition of the connective tissue, with increased functional activity of the cells, the ensuing fibrous hyperplasia is to be regarded as of inflammatory origin; where, on the other hand, local injury is not recognisable as the primary cause of the cell-growth, the hyperplasia must be held to be non-inflammatory. In passive congestion, obstructed lymph-flow, and increased nutrition consequent upon arterial change, as in the cases cited above, we can so far see no cause for the fibrous hyperplasia beyond altered conditions of nutrition, coupled with increased functional activity (strain); there has been no

primary lesion in the affected regions inducing the reaction. Such cases must be considered as non-inflammatory.

But while we lay down this distinction, we must impress upon the reader that the last word has by no means been said upon this matter, and that further research may cause a radical reconstruction of our opinions. At present our classification is the following :—

Forms of Fibrous Hyperplasia

A. *Inflammatory.*
   1. Productive.
   2. Replacement.
   3. Mixed.

B. *Neoplastic.*
   1. Transitional, of irritative origin (cheloid).
   2. Neoplastic proper, of unknown origin (true fibroma).

C. *Functional.*
   1. Arterial.
   2. Venous.
   3. Lymphatic.

VI.—Temperature Changes

Chapter 22.—Upon the Increased Temperature of Inflamed Areas

Very little has of late been added to our knowledge in this division of our subject: what is to be said appears now to be so well established that I need do little more than state the main conclusions. The long controversy that raged before these conclusions were fully accepted, and John Hunter's original views shown to be in the main correct, scarcely comes within the scope of this article.

1. The temperature of superficial regions is raised, it may be several degrees above the normal, by the onset of inflammatory hyperæmia.

2. The temperature of internal organs when inflamed may be raised above the normal, but undergoes no material increase beyond that of other unaffected internal organs tested at the same time.

3. The rise above the normal, which is often present, is an indication of the febrile state accompanying the inflammation, and not of locally increased heat-production. It is deserving of note in this connexion that botanists have demonstrated clearly that local injury in the higher plants is followed by a local rise of temperature which can only be the manifestation of local increased activities of cells. In animals it is quite possible, nay probable, that, where the irritation is not too severe, the increased metabolic changes in the cells tend towards katabolism and liberation of heat; but if so, this is so slight, and the heat is so rapidly diffused into the

circulating blood that thermometric measurements fail to give evidence of its existence.

4. The increased temperature of superficial areas when inflamed is due, not to the production of heat in the part, but to the increased quantity of blood passing through it. When the congestion is so great that stasis ensues, there may be actual decrease in the temperature of the part.

5. The maintenance of high external temperature may exert a favourable effect upon the duration and progress of specific inflammation. Thus Filehne (190) has shown that the course of experimental erysipelas in rabbits is more rapid and more benign when they are kept at a high temperature than at a low. We possess no clear evidence that this is due to the unfavourable effect of the heightened temperature on the growth of the microbes. Pasteur's well-known experiments (191) upon the production of anthrax in fowls (ordinarily insusceptible to this disease) by lowering their temperature can be explained on other grounds. We have abundant evidence that heightened temperature promotes vascular dilatation: the experiment of Filehne may therefore supply a further demonstration of the favourable effects of dilatation of the vessels and hyperæmia in the inflammatory process.

6. Low external temperature, or the application of cold to the surface, contracts the vessels: hence, upon the lines of what has already been said, it would appear that

(*a*) It is calculated to diminish the amount of exudation.

(*b*) It is calculated in consequence to diminish the pain associated with inflammation.

(*c*) It has no directly good effect upon inflammation due to the presence and growth of pathogenetic micro-organisms, but may have the reverse effect of preventing the fullest reaction on the part of the organism.

(*d*) Where the irritant does not itself grow and multiply, or present cumulative action, there the application of cold may not only be of no harm, but of positive advantage, by lessening the inflammatory reaction and preventing this, where extensive, from being itself a cause of further injury to surrounding tissues.

The increase of systemic heat will be considered in the article on Fever.

PART III.—On the Various Forms of Inflammation

Chapter 23.—Classification

The minute changes which characterise the process as it affects one or other organ, and the various specific forms, or, more accurately, grades of inflammation, will be fully described in special articles.

I have only to indicate more general causes and main varieties. To give a complete classification is impossible unless each separate tissue be taken in order, for each tissue presents peculiarities either in liability to inflammation or in the course assumed by the process. Even to attempt a classification in broad outline is beset with difficulties, for the inflammatory manifestation varies, not according to one or two series of causes, but according to four at least; the permutations are thus so numerous, and the appearances so varied, that to give an adequate scheme of classification would require a diagram in four dimensions. These four causes of variation are—

A. Nature of tissue affected. B. Position of tissue affected. C. Intensity of irritation, or, more correctly, ratio between resistant powers of the organism and intensity of the irritant. D. Nature of irritant.

A. Nature of Tissue affected.—As I have already shown in the first portion of this article, there is in the earlier stages of the process a difference in the reaction of vascular and non-vascular tissues, the one series exhibiting marked congestion and vascular disturbance, the other not. At a later stage, or in more chronic irritation, as new vessels invade the non-vascular areas, the changes in the two series do no doubt approximate; but in the earlier stages we may distinguish between an ordinary inflammation and "inflammatio sine inflammatione."

The relative denseness and compactness of the tissues also introduce characteristic alterations: a dense tissue, such as bone, does not show the signs of reaction to injury to nearly the same extent as does a loose tissue—such as the omentum, for example—thus, in the former there may be a process almost as atypical as in non-vascular areas. The rigid framework of a tissue like bone prevents great vascular dilatation and exudation, but at the same time may be the seat of great pain due to pressure of the confined exudate upon the nerve-endings. The loose connective tissue of a structure like the omentum, on the other hand, permits great exudation with little or no pain. These considerations tend to negative the view recently expressed that inflammatory pain is mainly due to the effect of alteration in the chemical composition of the exudate upon the nerve-endings.

The influence of structure is well seen in comparing the course of inflammation affecting cutaneous, mucous, and serous surfaces respectively. Where we have to deal with cutaneous surfaces, or surfaces formed of squamous epithelium, there the increased exudation, and the resistance offered by the layers of flattened cells to the free exit of the exuded fluid, lead towards the formation of vesicles or blisters. In the case of serous surfaces, which form the walls of a moist cavity, the irritant, affecting primarily but one portion of the surface, is very likely to be borne into the cavity with the exudate and to set up an inflammation extending over a very large portion of the surface. Mucous and cutaneous surfaces, which are not thus the boundaries of cavities, exhibit a more marked disposition to the production of localised inflammation and of ulcers; the superficial layers indeed of a well-formed epithelium or

mucous membrane, by the protective powers of their cells, form a defence against irritation from without: thus the superficial exudate from a region of local inflammation cannot easily produce a superficial extension of the process.

Not only the nature of the tissues, but their function also, profoundly affect the character of the inflammatory manifestation. Thus, excretory organs, by the very nature of their function, during the attempt to remove noxious substances from the system, are especially liable to generalised *parenchymatous* inflammations,—the irritation not being local, but affecting at the same time all the cells whose part it is to take up and excrete the irritant bodies.

B. The Position of Tissues.—It is difficult to consider the position and relationship of tissues as they affect the inflammatory manifestations, without continually touching upon their structure. Nevertheless, the two, though very closely connected, do not go hand in hand.

A familiar instance of modification in form brought about by position is to be seen in the result of suppurative inflammation—in the development of *ulcerous* conditions when the process affects free surfaces, of *abscesses* when it attacks deeper tissues. The process in the two cases is virtually the same: there is the same abundant determination of leucocytes, the same degeneration of them into pus. Yet apart from the gross difference in form, there are minor differences between the two. There is, for instance, relatively much more serous exudation from the free surface of an ulcer than there is into and around an abscess. As a general rule, inflamed tissues near a free surface are the seat of more abundant exudation. Of this liability for free surfaces to be the seat of serous inflammation I have already spoken. The skin, with its thick dermal layer, affords a good example: when the full suppurative stage is not reached, inflammation affecting the outermost layers of the derma is most often of a vesicular or œdematous character; when it affects the deeper layers of the derma the serous infiltration is less evident.

Yet another example of the influence of position in modifying form is seen in enteric fever. In this malady, the lymphoid tissue forming Peyer's patches becomes the seat of excessive cellular infiltration and proliferation, undergoes necrosis, and is cast off, leaving the well-known ulcers. The lymphoid tissue of the neighbouring mesenteric glands likewise undergoes great infiltration and enlargement, but necrosis rarely implicates the whole of a gland: notwithstanding the previous extensive inflammation, the glands commonly recover their normal appearance and size.

Beyond this there are few broad principles to be laid down concerning the relationship between forms of inflammation and position that do not essentially depend upon the structure and functions of the tissues. Much can be said concerning the intimate connexion between position and liability to inflammation; but this and the allied and most important subject of the protective mechanisms of sundry tissues against injury are away from our present point.

C. The Relative Intensity of the Irritant is a more frequent and potent cause of variation. I have already in several places referred to the ratio between the resistant powers of cells and the intensity or virulence of the irritant as it affects the inflammatory process, and have shown how much that was previously vague has been made clear by bacteriological research; while, at the same time, it has brought home the truth that there is a single process of inflammation, the manifestations of which while varying merge insensibly the one into the other.

Broadly speaking, it may be stated, as a result of these studies, that, *cæteris paribus*, increased virulence of any given microbe or diminished power of resistance on the part of the organism or of the tissues, leads to corresponding alterations in the phenomena of inflammation at the region of inoculation; and *vice versa*.

Thus, if a pathogenetic microbe, such as that of anthrax or erysipelas, be greatly attenuated, the effects of inoculation into the subcutaneous tissues may be scarcely recognisable. If the attenuation be not so extreme, some hyperæmia, a determination of leucocytes, and, relatively, very little exudation, will be seen; and in the course of a day or two all traces of inflammation may have disappeared. With slightly more virulent microbes the migration of leucocytes may be followed by their breaking down and consequent abscess-formation; with further increase of intensity of action the migration of leucocytes may be wanting, while the exudation extends and the inflammation rapidly spreads and leads to a bacteriæmia. A like series of changes is observable if the strength of virus be constant and animals more and more susceptible (or less and less refractory) be inoculated.

The variation in tubercular lesions, from isolated dense fibroid masses to loosely formed cell-accumulations and diffuse tubercular inflammation, is evidently inexplicable on this law. The law holds good also, not merely for bacterial products, but for other irritants. The effect of croton oil varies with the strength of the solution applied; and, as shown by Samuel, according to the condition of the animal. The same is true of abrin and other vegetable extracts.

Turning to physical irritants, while here the intensity of the irritant alone or almost alone is called into play, numerous examples can be given of the effects of variation in this one respect upon the inflammatory manifestation—effects of cold, for instance, varying from chilblain through inflammatory œdema to gangrene; of heat varying from hyperæmia through vesicular inflammation to complete destruction of tissue; and, again, effects of caustic substances. In this era of aseptic surgery we may forget what was well known to the last generation of surgeons, that caustic substances may be employed either to originate a benign and reparative inflammation (as in the case of indolent ulcers); or, in larger quantities or greater intensity, to bring about a state in which the death of the tissue-elements is far in excess of the subsequent repair. Thus then, according to the above-mentioned ratio, inflammation in a tissue may vary by insensible gradations from a mere hyperæmia up

to a spreading suppurative or gangrenous process; and from a purely local manifestation to the development of what may be termed an inflammation of the whole organism.

D. The Nature of the Irritant.—It is clear, then, that it is impossible to base a classification upon the nature of the irritant: the attempt to mark off sharply the inflammations caused by mechanical and chemical noxæ from those produced by bacteria and their products must be given up. Hüter's proposition that suppuration can only be induced by microbes has been repeatedly shown to be erroneous. Thanks more especially to the researches of Councilman, Leber, Grawitz and de Bary, and Straus (many more names might be mentioned in this connexion), we now know that many chemical substances are capable of causing pus-formation. Among these may be mentioned turpentine, croton oil, mercury, copper, and silver nitrate. While this is so, it must be borne in mind that under ordinary conditions these substances very rarely act upon the organism in a state of sufficient concentration to be pyogenetic. Thus, while it is impossible to make a sharp line of demarcation between bacterial and chemical irritants, it holds true in the main for man that suppurative disease is an indication of the presence and growth of microbes. On the other hand, although this pyogenetic property is not confined to microbes and their products, yet among microbes it is not the common property of all. Some, like the bacillus of tetanus, never in themselves induce pus-formation: others, like the bacillus of tuberculosis, lead characteristically to tissue-growth and the formation of inflammatory neoplasms rather than to pus-formation. Even among those which, like the micrococci, are highly pyogenetic, the formation of abscesses only occurs when there is a definite relationship between the virulence of the microbe and the resistance of the organism. The reverse is equally true, that numerous microbes, not specially pyogenetic, produce pus under peculiar conditions. Thus, the bacillus typhosus, when it multiplies in the middle ear, induces a suppurative otitis, and is further capable of originating a suppurative arthritis and the formation of abscesses in various tissues.

In fact, under varying conditions the same microbe can induce very various forms of inflammation. Thus, Charrin (192) has shown that the B. pyocyaneus and its products are capable of inducing in one organ—the kidney—pathological conditions so diverse as acute, chronic, parenchymatous, interstitial, and thrombotic nephritis, with, in addition, cyst-formation and amyloid degeneration.[1] This same microbe can induce acute suppuration in the anterior chamber of the eye; and when inoculated into the blood cause a hæmorrhagic inflammation of the serous surfaces. Hence we can proceed farther and state that no strict classification of inflammation can be made according to the nature of the bacterial irritants; it is, however, possible to make a general grouping of those affecting man, as follows:—

[1] These changes are comparable with the diverse conditions of the kidney in the human being brought about by the scarlatinal virus.

(i.) Micro-organisms characteristically leading to pus- and abscess-formation—Staphylococci and streptococcus pyogenes, B. anthracis.

(ii.) Those leading to abundant exudation with necrosis—B. of malignant œdema.

(iii.) Those leading to cellular infiltration without usually causing abscess formation—B. typhosus, M. gonorrhœæ, B. diphtheriæ, etc.

(iv.) Those inducing characteristically the development of inflammatory neoplasms—B. tuberculosis, B. pseudo-tuberculosis, B. mallei, Actinomyces, Aspergillus fumigatus.

Similarly, chemical substances may roughly be grouped into—

(*a*) Substances causing so slight an irritation when introduced into the organism as to induce cellular overgrowth only in their immediate neighbourhood—such as bland foreign bodies, bullets, etc.; inhaled particles of coal, stone, iron, and the like, conveyed into the pulmonary lymphatics.

(*b*) Substances leading to vesicular inflammation, for example, blistering agents, such as cantharides. (This result, however, depends more upon the position than the nature of the irritant.)

(*c*) Substances leading to cell-necrosis, followed by the formation of granulation-tissue—caustic agents.

(*d*) Substances leading to cell-necrosis and suppuration, such as copper, mercury, mineral acids, etc. (a very rare result in man).

These lists, from the considerations given above, are necessarily unsatisfactory and imperfect.

Other Considerations.—Among other factors modifying the inflammatory process may be mentioned the duration of the action of the irritant, which of necessity must modify the extent of the manifestations of disturbance in the tissues. A simple aseptic incision, for example, leads to a much milder and slighter series of changes than do the prolonged presence and growth of the tubercle bacillus. And in general it may be stated that mechanical causes of injury set up the simplest forms of inflammation—those unaccompanied by suppuration, unless secondary infection ensues. To state, as laid down by some authorities, that mechanical injuries do not induce inflammation, is wholly opposed to the conception of the process here accepted. Even the simplest fracture of a bone, for instance, is followed by dilatation of the vessels of the surrounding parts, by exudation, diapedesis of leucocytes, and indeed by all the cardinal symptoms whether of the old or the more modern school. While at first it might appear an easy matter to name case after case where the irritant has but a momentary action, upon further consideration it is found that, in the majority of cases of purely mechanical injury, this is not the case; or, to express the matter more exactly, in the case of physical injuries, it is not the act of wounding that causes the inflammation, but the damage inflicted upon the cells of the tissues; as, to a very large extent, inflammation is set up by the products of the injured and destroyed cells. A bone may be suddenly broken, and, nevertheless, even in the most favourable circumstances, pain,

swelling, and congestion may affect the region of fracture for several days. One or other region of the body may be rapidly frozen : the inflammation does not manifest itself till after the physical agent has ceased to act, but it continues for hours, and even for days.

There are, moreover, physical irritants of another nature producing definitely chronic inflammation ; I refer to foreign bodies which have gained an entrance into the system. These if bland in themselves may nevertheless cause irritation. A good example of the extensive inflammation which such bodies may set up is seen in the dense fibrous interstitial tubercular masses developed in the lungs of stone-masons around fine silicious particles carried into the lymphatics from the alveoli.

From such examples it will be evident that no satisfactory distinctions between bacterial irritants on the one hand, and physical irritants on the other, can be founded on the duration of irritation. This factor plays no easily recognised part in determining the various forms of inflammation, and consequently I have forborne to place it in the list at the beginning of this chapter.

In thus passing rapidly over the influence of each of the four main causes of variation I have of necessity excluded sundry forms of inflammation due to the combined action of two or more. There are, for instance, such well-marked forms as the *catarrhal* and *croupous*, due to the interaction of all four factors: embolic inflammation and lymphangitis have also been passed over ; these, however, are not so much forms of inflammation as inflammatory processes occurring in special regions as a result of special methods of conveyance of the irritants.

The factors then are so many, and their interaction so varied, that anything approaching to an orderly classification is hopeless. What I have here written must be regarded, not as an attempt to formulate such a classification, but as an attempt to indicate briefly how the nature and position of the tissues and the nature and intensity of the irritant bring about modifications in the process of inflammation.

Chapter 24.—On Systemic Changes consequent upon Inflammation

The results of an acute local inflammatory process are not confined to the immediate locality, but associated alterations in the system at large have long been recognised ; yet while recognised these systemic changes have been but little studied : I cannot pass the matter over in silence, but my setting forth of it must necessarily be very brief and imperfect.

I cannot here say more upon the effect of local irritation on the nervous system than that, apart from direct reflex action leading to changes of nervous origin in the region of injury and the reflexes affecting associated regions, the higher centres, and through them the system at large, may become affected by paths that it is not always easy to trace.

The disturbances of the nervous system which accompany local injury ın be but vaguely and indefinitely described. As regards the secondary ffects, the most suggestive work of Prof. Roy and Dr. Cobbett (193) ıd more recently of Crile (194) upon *Shock*, indicate that there is here a ch field for yet further research. Of the changes in the general circula- on, and more especially in the circulating blood, thanks to the observations Von Limbeck (33), Rieder (195), Löwit (196), and Prof. Sherrington 97) we possess more exact knowledge; in acute local inflammation of ome extent the circulating blood becomes inspissated: by exuda- on it loses some of its plasma, while the more solid constituents— ıe red corpuscles—do not escape. The amount of fluid lost to the rculation is not equalised by increased entrance of lymph into the rculation: in one experiment of Prof. Sherrington the blood remained ooplasmic (that is, its specific gravity remained heightened) for more ıan sixty hours after the infliction of injury. This apoplasmia or minution in the relative amount of plasma in the blood appears to epend in some measure upon the extent of the vascular area involved in ıe inflammation; for example, Prof. Sherrington shows that when both eet are involved, by plunging the limbs in water at 52° C., the ooplasmia is more severe than in experiments affecting one foot only. nother well-marked change in the blood concerns the leucocytes. As ıspected by Löwit and proved by Prof. Sherrington, there is, in some rms of inflammation at least, a primary diminution in the number of ucocytes per unit volume of blood (leucopenia), followed by a marked crease in the number of leucocytes in the blood (leucocytosis). The ımber of leucocytes was in some instances increased sevenfold. In the ucopenia of inflammation, the diminution is chiefly confined to the nely granular leucocytes—the finely granular oxyphil cells of Prof. anthack and Mr. Hardy. These observations of Prof. Sherrington are onfirmed by the observations of Everard, Demoor, and Massart (198).

Whether the diminution be due to disintegration, or to collection some area of the circulation, is not yet wholly determined; the oservations of Prof. Muir and others favour the latter view, and indicate e lungs as regions in which the accumulation occurs. The leucocytosis ay become obvious within an hour after the establishment of a local sion; and it may be prolonged for several days, even in cases where the jury has been of a mechanical nature. Here, again, according to most oservers, it is chiefly the polymorphonuclear or finely granular oxyphil lls which increase in numbers. It is interesting to note that coinci- ently the coarsely granular eosinophil cells appear to undergo great minution (77). I can do no more than point out the existence of these ood changes, and further that changes in the number of leucocytes in e blood are certainly not accounted for by the number passing from the ood into the inflamed area. It would seem that local inflammation in me way brings about an over-stimulation of lymphoid tissue, notably at of the bone-marrow, whereby an increased number of leucocytes are oured into the blood; or it may initiate increased proliferation of the

leucocytes already in the circulation; but how one or other of these effects is produced is at present unknown. Certainly the direct introduction of the products of bacterial growth into the circulating blood may lead to a more or less pronounced and rapid diminution of the number of leucocytes in the blood, and this diminution, as shown by Löwit, may be preliminary to a subsequent increase.

The further important general disturbance associated with local injury, more especially when of bacterial origin, namely, the occurrence of fever, are described in the following article. Bacteriological studies lead to the conclusion that traumatic fever, at any rate, is largely due to the diffusion in the blood-stream of soluble bacterial products, and of the products of tissue-destruction derived from the inflammatory focus.

Chapter 25.—On Adaptation: Conclusion

It will be seen that the picture of inflammation here given is very different from the old view in which the dominating idea was that inflammation is essentially an injurious process leading to cell- and tissue-destruction. Here we regard the *irritant* as capable of causing cell- and tissue-destruction, and so long as the irritant is in action so long may this destruction continue. But inflammation itself we regard as the series and sum of the reactive processes set up in the tissues, and then bringing about, not destruction, but the very reverse. Taking as our definition, that inflammation is the response or reaction to injury, we are inevitably led to see that this response results in counteracting, or more exactly in tending to counteract, the deleterious effects of the irritant; the inflammatory process tends towards repair. It may not result in repair, for, as we have pointed out in several instances, too often the reaction is either inadequate or excessive. The exudation may possess but slight bactericidal powers, or may be poured out in such quantities that the microbic irritant, instead of being retained in the region of injury, is conveyed outside that region; the wandering cells, instead of destroying, may undergo destruction; they may incorporate bacteria, but not be able to annihilate them; the fixed cells may either form an incomplete cicatrix, or continue to proliferate in excess. Attempt at repair is not repair. Notwithstanding, studying the various factors involved, it is forced more and more upon us that each tends in one definite direction, and the sum of the process is reparative.

This conception of the process of inflammation has met with considerable opposition. It is urged that, to consider inflammation as an attempt at repair is teleological, *i.e.* is to assume that each reaction in the process is, in itself, purposeful. And, carrying this objection to its ultimate end, "you conceive," say the critics, "that the leucocyte is endowed with intelligence so that it recognises in the microbe a foe to the organism; scents it from afar; hunts, seizes and digests it, and then, its duty done, its mission in life fulfilled, it withdraws its pseudopodia and dies contentedly."

It is needless to say that we hold no such views regarding the intelligence of the leucocyte. At the same time, we unhesitatingly regard inflammation as purposeful—every whit as much as we regard the iris, with its contraction and dilatation under different intensities of light, as subserving a purpose, or the acts of feeding and digesting as being with purpose. Inflammation is a physiological process in so far as it is the calling into action, in response to accustomed stimuli, of properties normally possessed by the tissue; it is a pathological process in so far that, while the stimuli are in kind not different from normal stimuli, in intensity they are greater. If we admit physiological purpose, we must admit pathological. This may, indeed, be laid down regarding all pathological conditions, namely, that in them we are not dealing with the effects of new and unaccustomed factors, but with the ordinary factors falling upon the tissues in an abnormal way, being either deficient or excessive in their action. Within physiological limits, the reaction to a given stimulus is nicely balanced and adequate; when the stimulus is excessive, the reaction is liable to be imperfect. The iris accommodates and adequately protects the retina within certain limits, but, if the eye be exposed to too intense a light, the iris fails to arrest all the rays and the retina suffers. And so it is that, in inflammation, when the stimuli are excessive and so have become irritants, the tendency is for the reaction not to be perfectly balanced, and the ultimate result to be an incomplete counteraction of the disturbance. But, to repeat, if we recognise purpose in the one set of cases, we must recognise it in the other.

All, it will be seen, depends upon what is our conception of "purpose" in vital phenomena. That conception is teleological if and when we regard it as primary—as what may be termed an intelligent endeavour on the part of the tissue to accomplish a certain object—a predetermined end. To suppose that, in inflammation, the vessels dilate and bring about increased exudation *in order to* flush out the irritant, is an utterly wrong and baseless idea. If, on the other hand, our conception is along these lines—that in the course of evolution those individuals survived who, by chance, let us say, happened to manifest this reaction on the part of their vessels in response to stimuli of a certain order, whereas those who did not were more unfavourably placed and so succumbed; that they conveyed the same power to their descendants who also possessed this advantage over individuals incapable of affording the reaction; then we can conceive the development of a race possessing a mechanism for countering a given stimulus by a given reaction, a race in which provision is made, or gained, for dealing with a given order of events; then it will be seen that what primarily is accidental becomes secondarily purposeful through the survival of the fittest and the inheritance of defensive acquirements. The tissues thus become prepared to respond to certain alterations in their environment. In other words, "natural selection" renders what was primarily accidental, secondarily purposeful.

The whole process of inflammation is an exemplification of "adaptation," and we would strongly commend the address by Prof. Welch (199) upon this subject to those desirous of gaining a right point of view regarding pathological processes in general. For living matter to survive, it must be adapted to its environment, and this, in the first place, happens through inheritance, through the survival of the fittest, along the lines laid down above.

Yet, in the study of inflammation, we are compelled to recognise, not merely inherited, but also individual adaptation. We cannot otherwise explain why it is that bacteria, which at first exhibit active local growth within the tissues, become eventually destroyed on the resolution of the inflammatory state, unless we acknowledge that the cells, or certain of them, acquire and, it must be, transmit, increased bacteriolytic and antitoxic properties. The facts gained regarding the development of immunity—the presence in the body-fluids of the immunised animal of substances inimical to the infective agents, which are absent, or present in but minimal amounts, in the fluids of the untreated animal—all demonstrate this individual adaptation. At the present time, indeed, workers all over the civilised world are busy in researches bearing upon this very subject, the production and mode of action of what may be termed, generically, anti-bodies.

Here I can do little more than mention certain general laws which seem to be at work in bringing about, or favouring, individual adaptation.

1. The first is that of *reserve force.* No cell—and no tissue—normally is in action to the limit of its powers; on the contrary, normal activity is far below what the cell is capable of performing. In other words, normal stimuli do not induce a maximal reaction, and, therefore, irritants—excessive stimuli—up to a certain limit, do not overwork, and do not lead to disintegration of the cell. Perhaps the greatest difficulty encountered by most students of medicine in accepting the facts of phagocytosis lies in this, that, regarding the tissues as normally sterile, they cannot comprehend the assumption of what appear to be totally new properties by the leucocytes and other cells in inflammation and infection, namely, the assumption, as they regard it, of phagocytic powers and the taking up of pathogenetic bacteria. But, as a matter of fact, this is no new property. Throughout life the cells are engaged in digesting bacteria. We find phagocytic leucocytes passing out and free upon mucous surfaces—any smear or swab from the pharynx will show these leucocytes with their contained bacteria. As Dr. Ruffer (200), Nicholls (201), and others have shown, bacteria are to be seen in the lymph-glands and along the lymphatic channels of healthy animals, and these, most often, within cells. As Ford (202), working in my laboratory, has demonstrated, using the fullest precautions against contamination, bacteria can be cultivated from the liver and kidneys of more than 50 per cent of the apparently healthy animals of the laboratory: and that the bacteria so obtained are not contaminations is proved by the remarkable regularity with which each different species presents a

fferent bacterial flora. Having followed Ford's observations and seen e care with which they were conducted, I cannot accept the observa-ons of those who refute his work. As Wroszczk (203) has recently own, if animals be fed with non-pathogenetic germs, or germs setting no recognisable intestinal disturbances, colonies of the species so in-ted are, later, to be gained from the various organs of the apparently althy animals. The tissues are *potentially* sterile; that is, the leuco-tes and other phagocytic cells are, throughout life, engaged in destroy-g bacteria which have gained occasional entrance into the tissues (204). hen a few intensely virulent bacteria gain this entrance, or a large mber of a less virulent form manage to grow in some one or other ality, and thus set up inflammatory changes, the above-mentioned erve force in the phagocytic cells comes into play and permits these ls to take up and digest the greater numbers or the more toxic forms.

2. The second law is that of *accustomance.* A cell not actually stroyed by any deleterious agency is apt to become accustomed to the esence and action of that agency. What is the basis of this accustom-e it is difficult to say, though it is not difficult to suggest a hypothesis hypotheses. Here I simply state that this is an observed law, a law t exemplified in what has been made out regarding the conversion of egative into a positive chemiotaxis.

3. The third and very important law, somewhat closely allied to the , is that of *habit*, or, as Fraser Harris (205) has termed it, "vital rtia." According to this law, when once, through a given stimulus, ertain series of molecular changes is set up in a cell, those changes liable to continue after the stimulus has ceased, and, if the stimulus sufficiently strong or sufficiently often repeated, the cell acquires the it, or property, of setting in action a particular series of molecular nges after a minimal stimulation. This is, perhaps, best exemplified connexion with our subject in the production of antitoxins. It is nd that, once the diphtheric toxin, for instance, has stimulated the s of the organism to produce antitoxins, that production continues is wholly out of proportion to the amount of toxin introduced; le, similarly, once an animal has gained full immunity against any anism, it only needs the introduction of that micro-organism into the em to induce an immediate reaction, whereas previously days or ks had been required for accustomance and counteraction to be quately developed.

Hence, to sum up, while I would not give this as a definition (as I in a previous edition), for I see the force of Dr. Ainley Walker's ument that, in a definition, one should state what a thing is and not t it tends to bring about,—my conception of inflammation, from all considerations here laid down, must be that it *is the series of changes ituting the local manifestation of the attempt at repair of actual or referred y to a part, or, briefly, as the local attempt at repair of actual or referred ry.*

And in conclusion let me lay stress upon what I regard as the main outcome of this essay. In studying the reactions of the organism to injury, we must be impressed by the multifariousness of natural processes; the end may be attained, not in one way only, but in many. It is not by cells of one order alone—by phagocytes—or by leucocytes in general and only leucocytes, or merely by the reaction on the part of the fixed cells of the tissue, or by vascular changes alone, or by altered temperature, or solely by the chemical and mechanical action of the exudate that repair is effected. All means are employed to antagonise the irritant and to effect healing. The cells of the body, fixed and free, play their part; the nervous system aids the process; the bodily humours render efficient help; modifications in the vessel-walls and blood-stream are valuable auxiliaries. Diverse processes are employed, now one more particularly, now another, according to the needs of the moment, but none exclusively.

So diverse are the opinions of pathologists upon many branches of this subject of inflammation, and so great is the amount of recent research, that I can neither hope that all the conclusions here set down will gain acceptance, nor that in these pages, inevitably condensed as they are, I have succeeded in recognising and duly acknowledging all work of primary importance. In the rapid progress of our science, much, it may be, that is here set forth will be modified. Nevertheless I hold that the conception of the inflammatory process indicated in this article is that which embraces the largest number of like phenomena, and excludes most satisfactorily those which if associated are unessential; and that it is by the study of cellular pathology in its strictest sense that the surest advance has been and is to be made in our knowledge of this the dominating process in disease.

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FEVER

HISTORICAL RETROSPECT, by Sir J. BURDON-SANDERSON, Bart., M.D., F.R.S.

PHYSIOLOGICAL CONSIDERATIONS, by M. S. PEMBREY, M.A., M.D.

CLINICAL CONSIDERATIONS AND TREATMENT, by W. HALE WHITE, M.D., F.R.C.P.

IN the first and introductory section of this article the subject is treated in the order of time: beginning with Virchow an account is given of his doctrine of fever; then follow the doctrines of his most distinguished contemporaries and successors in the field of Pathology—Traube, Liebermeister, Senator, Leyden, Cohnheim. The second part, entitled "Physiological Considerations," deals with the subject of fever under the following heads:—Temperature, Regulation of Temperature, Production of Heat, Respiratory Exchange as a Measure of the Production of Heat, Loss of Heat, Metabolism, Secretion and Excretion, Respiration, Circulation, Nervous System, Theory of Fever. In the concluding part, entitled "Clinical Considerations and Treatment," the subject is considered from the point of view of practical medicine It comprises sections on the causes, symptoms, prognosis, and treatment of fever.

PART I.—HISTORICAL RETROSPECT, 1850-1883

By Sir J. BURDON-SANDERSON, Bart, M.D., F.R.S.

Of the scientific conceptions relating to the origin and nature of diseases, out of which the science of pathology, as we now understand it,

was built about sixty years ago by Virchow and his immediate predecessors, none were more fundamental than those relating to fever and inflammation. These conceptions were so entirely unconnected with the hypotheses which had previously been taught under the name of General Pathology that, in tracing the development of our present knowledge, no advantage would be gained in going farther back in our retrospect than the middle of the nineteenth century.

Johannes Müller—whose teaching was the spring of the great movement in all matters relating to the nature of disease, of which Virchow was the exponent—had compared fever to a reflex process of which the phenomena were the response to stimulation of the spinal cord by means of "organic nerves." About the same time the discovery by E. H. Weber of the inhibitory nerve of the heart had suggested new ideas as to the way in which the central nervous system governs the circulation. He had shown that this influence is exercised, so far as the heart is concerned, by two channels of which the actions are antagonistic, that of the one exciting, that of the other quelling. As regards the blood-vessels, constricting or tonic nerves had been discovered, but it remained for Schiff to find out that there are also nerves which control vascular tone.

Out of the principle of antagonism which the discovery of Weber involves, there developed in the fertile mind of Virchow the notion (he declined to call it a theory)[1] of *fever as a neurosis*, which was expressed in his treatise on Pathology published in 1853. Students of pathology were taught by him for the first time that fever was not an over-active, but a paralytic state; that its excesses—the over-action of the heart, the "tension of the whole vascular system," "the abnormal production of heat"—were the expression of *failure of control*, of weakness rather than strength. But of the way in which this control was exercised, or how it failed, he could at that time give no explanation; he contented himself with suggesting that the "moderating centres" could influence not merely the heart and blood-vessels, but also the "*Stoffwechsel*," what we now call metabolism. According to Virchow, the nervous system in fever loses its control over all the organic processes, and in this the essence of the febrile state consists.

In 1855 Traube (1) made the discovery that in fever *the elimination of nitrogen is increased*.[2] This seemed to indicate that if fever be a neurosis, there must either be "trophic nerves" by which the chemical processes of the organism can be controlled—for how else could an affection of the nervous system bring about tissue-disintegration?—or we must suppose, as did Dr. Parkes, that the cause of fever, the catalytic agent of which Virchow wrote, directly attacks the tissues. Traube's explanation, however, differed from both of these, for he thought that the admitted increase of disintegration of albuminous compounds was

[1] "Das Alles ist gewiss sehr wenig und genügt auch nicht annähernd um eine Theorie darauf zu bauen."—Virchow, *Handb. der Pathol.* p. 36.

[2] It is noteworthy that the paper in which this discovery was made known is one of three pages.

secondary to the disturbance of the circulation. Of the nature of this disturbance he framed an hypothesis which, whether true or not, exercised a greater influence than any other on the progress of investigation. It may be shortly stated as follows:—Traube, like Virchow, assumes the existence of a fever-producing agent, but holds that its action is exercised, not on inhibitory, but on tonic vasomotor nerves; that the first physiological result of this influence is contraction of the peripheral arterioles, and consequently a rapidly diminished flow of blood to the surface; the temperature of the skin declines, and a rapid rise of internal temperature follows. To the increase of the difference between the external and internal temperatures he attributes the rigor of accession. The decline of temperature is due to nothing more than the cessation of the vascular spasm.

So hard and fast a statement of what happens in fever was found difficult to accept; and it soon appeared that it was not in accordance with observation. As regards the initial stage its utility as a "working hypothesis" consisted in this, that it gave prominence to the influence of the nervous system on the liberation of heat at the surface, and to the adjustments by which this liberation is adapted to the requirements of the organism; thus investigation was guided in a direction which the event has proved to be the right one.

Liebermeister was the first pathologist who attempted to investigate fever calorimetrically, the outcome of his work being first to demonstrate that even when the surface-loss is entirely annulled by raising the temperature of the environment to such a point that no heat is parted with, the increase of bodily temperature is not so rapid as in the initial stage of many fevers; and that, consequently, the latter could not be explained on Traube's principle; secondly, to give prominence to two doctrines of his own, which for a long time were very generally accepted. Liebermeister's doctrines were—(1) that in fever, as in health, constancy of temperature is ensured by the adaptation of production to discharge, not of discharge to production, as Traube taught: and (2) that in fever bodily temperature is regulated in the same way as in health, with this difference, that the norma has become several degrees higher. In fever the organism, according to Liebermeister, strives not towards the temperature 98·4° F., but towards 104° or 106°, as the case may be. Liebermeister's inference from his experiments, that arrest of surface-loss is inadequate to produce pyrexia, will not bear experimental criticism. To the second of the hypotheses referred to above greater interest attaches, because if illogical in form, it conceals an important truth. An abnormal norma may be a contradiction in terms, but the fact that the bodily temperature in continued fever approaches a certain limit which it does not tend to exceed, is one which can scarcely be disputed.[1]

[1] There are many distinguished pathologists who still hold to Liebermeister's doctrine that in fever the temperature is adjusted to a new norma. The points which seem to support it may be exemplified in the following experiment:—

It is possible either to raise or to depress the temperature of a healthy person by gradually cooling or warming the water of a warm bath in which he is placed. If by this

At this point the subject was taken up by Senator, the most successful, if not the ablest, of all the investigators of fever. We have seen that although Traube and Liebermeister differed very widely in their views, they agreed with Virchow in regarding fever as a disorder of that function of the nervous system by which constancy of temperature is maintained—the function of thermotaxis. Traube, being both a physiologist and a physician, was guided by the application of physiological inferences to clinical facts, Liebermeister very largely by observations relating to the treatment of fever by the tepid bath. Both recognised regulating centres, but as regards the way in which they act their views were antagonistic; the one relied on vasomotor nerves, the other on the control of heat-producing chemical processes by the nervous system. To Senator it appeared that the time had come for investigating the subject from all sides, experimental and clinical. Fever comprehends vascular, thermal, and metabolic phenomena, and no investigation seemed likely to be of value unless all three were dealt with. In the laboratory, Senator compared for the first time the discharge of heat of animals in which fever had been produced artificially, with the previous heat-loss of the same animal and with the heat-loss after recovery, employing, at the same time, the best methods then available for measuring the respiratory exchange and the elimination of nitrogen. One of the most noteworthy results was that, while the nitrogenous waste was considerably increased, there was no increase whatever of the consumption of fat, and no evidence of any greater increase of the respiratory exchange than could fairly be attributed to the existence in fever of conditions more favourable to the discharge of carbonic acid gas. As regards the discharge of heat, measured calorimetrically by a method far more accurate than that of Liebermeister, the results were negative. In the initial stage the surface heat-loss appeared to be diminished, but it could be ascertained that this diminution was compensated for later. In respect of the discharge of nitrogen, Senator's clinical observations confirmed and extended what had previously been observed, and showed in this respect a complete correspondence between natural and artificial fever. He estimated the rate of elimination of nitrogen in many instances to be more than double, *i.e.* to be increased in a degree out of all proportion to any increase which could be supposed to take place in the rate of heat-production.

At the time that Senator published his *Researches on the Process of Fever* (1873), Leyden was engaged in clinical investigations of the same subject (4), with results which differed from Senator's in some points of importance. The absence in animals of any marked increase of the

means the temperature of his body is depressed as much as ½ degree F. he shivers, if raised to the same amount he perspires. Repeating the experiment on a fever patient a similar result is obtained, with this difference, that if the temperature is say 104° F., he shivers at 103·7° and perspires at 104·3; whereas the healthy person, whose normal temperature is 98·8°, shivers at 98·3° and sweats at 99·2°. The explanation is that it is the change of temperature that produces the reaction, and the direction which determines its character—shivering if it is descending, sweating if it is ascending.

respiratory discharge of water and carbon dioxide had led Senator to conclude that in fever the only essential change in metabolism relates to the increased disintegration of proteid. On this point, however, Senator was for the most part guided by experiments on animals. Leyden, therefore, directed his efforts to investigation of the respiratory exchange and of thermogenesis in man. Considering that in continued fever there is no obvious indication of increased thermolysis, it was desirable to test this by more exact observation. For this purpose he employed a method of calorimetry which can be used clinically without inconvenience to the patient. Enclosing a limb in a cylindrical calorimetrical chamber, he estimated the loss of heat by escape of water, evaporation and radiation of the limb in relation to the surface, and calculated therefrom the whole surface-loss of the body, with the result that in fever, even when there is no visible perspiration, the thermolysis may be 40 per cent greater than in health. Having arrived at this result by clinical observation he had recourse to experiment (5), in the hope of confirming it by investigating the respiratory exchange in animals. The result was that in all cases the rise of temperature was accompanied by a corresponding increase of the discharge of carbon dioxide, the amount and duration of which was such as to preclude the possibility of attributing it to the greater activity of the respiratory movements. Shortly after the completion of these observations a series of experiments were made under Pflüger's direction (6), in which both the intake of oxygen and the output of carbon dioxide in normal and fevered animals were compared. These led this great physiologist to incline to Liebermeister's view, that normal regulation consists in the adaptation of production to discharge, and that increased production is an essential element of fever.

By way of conclusion to this retrospect I propose to state summarily how the question of fever presented itself to the two pathologists most competent to discuss it—Senator and Cohnheim.

Cohnheim, like Pflüger, in the Lecture on Fever which concludes the second volume of his *General Pathology*, sums up in favour of the doctrine that the nervous system presides over thermogenesis no less directly than over thermolysis. He accordingly seeks for evidence of increased production of heat throughout the whole febrile process.

In the initial stage, particularly when the rise of temperature is rapid, he admits that the cutaneous circulation is restricted, but not that this restriction is the cause of the rise. The sensation of chill is due to the suddenness of the diminution of temperature at the surface: when the change occurs gradually, it is absent. It is succeeded, in the fastigium, by a feeling of warmth, which means that the constricted vessels relax. He does not decide whether this is due to the intervention of inhibitory nerves or not, but emphasises, as evidence of vasomotor disturbance, that the more favourable state of the cutaneous circulation which characterises the beginning of the fastigium is liable to interruption by

the recurrence of chills, in which the skin becomes dry and the temperature tends to rise. The critical sweating is of course regarded by Cohnheim as a sign of increased flow of blood to the surface, which he does not hesitate to attribute to the influence of dilating nerves. Of cutaneous nerves of secretion little was known at the time when he wrote.

The remarkable law that in fever the diurnal range of variation is much greater than in health, Cohnheim attributes rather to fluctuations in thermogenesis than to changes in the circulation. This view seems to him supported by the consideration that in relapsing fever the efficient cause of pyrexia is plainly the presence of spirochætæ in the blood, and that these would influence thermogenesis rather than surface-loss. Had he known how close is the relation between the successive stages of ague and the life-history of the organism which causes it, he would have been confirmed in his conclusion that in periodical fevers the periodicity is a function of the cause, not of the disease.

In common with Virchow and all modern pathologists, Senator regards fever as a disorder of temperature-regulation, but for him the term regulation connotes "regulation by the cutaneous circulation." It is thermolysis, not thermogenesis, that is in the first instance disordered. This disorder is most marked in the initial stage, but exists in the fastigium, declining towards its close. Its presence manifests itself in dryness of the skin and maintenance of the high temperature, but of these two neither is caused by the other; both are directly dependent on the nervous system.

Finally, Senator regards the relation between the constituents of fever as a loose one; he believes there is no absolute inter-dependence of the disorder of nutrition and the pyrexia. The only invariable causal relation is that which subsists between pyrexia and disorder of the cutaneous circulation.

J. Burdon-Sanderson, 1896.

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Part II.—Physiological Considerations

By M. S. Pembrey, M.A., M.D.

Introduction—Temperature—Regulation of Temperature—Production of Heat—Respiratory Exchange as a Measure of Production of Heat—Loss of Heat—Metabolism—Secretion and Excretion—Respiration—Circulation—Nervous System—Theory of Fever—References.

Introduction.—Many diseases are accompanied by a complex process which is chiefly characterised by a disturbance in the regulation of the

temperature, a disturbance of such a kind that in most cases the heat of the body is abnormally high. To this disorder the term fever has been applied from the earliest times. The abnormal heat of the body impresses both the physician and the patient. Fever, however, is something more than a rise of temperature. In healthy men and animals during muscular exercise (1) the rectal temperature may be 101·3° F. (38·5° C.), or as high as that of a feverish patient; but it would be an error to say that they are ill, and it would be a misuse of terms to describe them as suffering from a "physiological" or "muscular fever"; they feel well and are well, the feverish patient, whose temperature is no higher, is ill and feels ill. On the other hand, a patient may be suffering from fever and yet show no high internal temperature, and upon this point evidence will be produced later to show that an *apyrexial fever*, often called a "non-febrile fever," must be recognised as much from a pathological as from a clinical point of view. It will also be necessary later to draw a further distinction between the high temperature of fever, *pyrexia*, and other abnormal conditions of high temperature, *hyperthermia*.

With the development of knowledge, the term fever has acquired two meanings: in one sense it stands for those complex departures from health, or diseases, the main feature of which is disturbance in the regulation of temperature consequent on the invasion of pathogenetic organisms; in another sense it implies only a rise of temperature. Some writers have attempted to restrict the use of the word to the first meaning, and to introduce the term pyrexia for the second. Here again confusion has arisen, for pyrexia has by other writers been used in a similar double sense, as shown by the term "apyrexial pyrexia," and yet other writers laying stress on the difference between fever and pyrexia have spoken of hyperthermia as pyrexia. It might be convenient if the term pyrexia were restricted to febrile hyperthermia, that is, to the high temperature observed during the process of fever.

It must be recognised that fever may be accompanied by no rise, but even by a fall in temperature, and that it is a complex process which is not to be distinguished by one sign alone. The increased nitrogenous waste is even a less satisfactory criterion than the course of the temperature, for it is obvious that fevers were recognised and studied long before anything was known about nitrogenous waste, and even at the present day the physician is in practice guided, among other signs, chiefly by the course of the patient's temperature and not by his nitrogenous waste.

Fever embraces far-reaching changes in the animal economy; its effects are shown upon the temperature, the exchange of material in the body, upon the circulation, the respiration, and the nervous system; in fact all parts of the body are disturbed, for the component parts react the one upon the other. Fever must be considered in relation to the departure from those complex interactions or adaptations of the various parts of the body which constitute health and enable the warm-blooded animal to maintain a fairly constant temperature under most varied

conditions; the discussion may be concluded by a consideration of the significance of fever.

Temperature.—The cardinal sign of fever, it is agreed, is the disturbance in the regulation of temperature; the indications of the thermometer yield, when it is properly employed, the most valuable evidence for diagnosis and prognosis. Unfortunately, however, this clinical method has been considered so simple that its application is often left to the nurse or even to the patient himself. Thus a high temperature is often overlooked when it is present, and at other times is discovered and considered pathological when it is within the range of health.

The first question to consider is the range of temperature in a healthy man, and how the internal heat of a patient suffering from fever departs therefrom. The mean daily temperature in health is about 98·2° F. (36·8° C.) and the range from 99·3° (37·4°) to 97·0° (36·1°), for the daily variation is about 2·3° (1·3°), with the maximum about six o'clock in the evening and the minimum about three o'clock in the early morning. These values (2) are for the rectal temperature. The indications yielded by a thermometer placed in the mouth are unreliable, and are generally too low, owing to the cooling of the mouth internally by breathing, and externally by the loss of heat from the cheeks by conduction, radiation, and the evaporation of sweat. The temperature observed in the axilla is also often too low, because the closure of the space is not sufficiently perfect or prolonged to raise the heat of the parts to that of an internal cavity of the body. It is obvious that convenience and reasons of delicacy are greatly in favour of the observation of the temperature in the mouth or axilla, but it must be recognised that the reading so obtained is often a degree or two lower than the temperature of the rectum, and that no constant correction can be applied. In short, a low or normal temperature in the mouth or axilla is not proof of the absence of pyrexia. During muscular exercise the temperature of the rectum or stream of urine may be as high as 101·3° F. (38·5° C.) in a healthy man without any ill effects or even discomfort; a similar rise has been proved to occur in animals. A rise of temperature during muscular work must, therefore, be considered physiological. The cessation of exercise is quickly followed by a fall of temperature to, and indeed below, the value found during rest. The characteristic of the healthy man is the perfection of his regulation of temperature; he compensates for a great range of external heat and cold; placed in a warm or cold bath, he can within certain limits so adjust his loss and production of heat that his internal temperature remains fairly constant. This regulation is effected by the nervous system. In marked contrast is the condition of the febrile patient (3); his regulation is imperfect, he cannot compensate for internal or external conditions, he is easily influenced by warm or cold baths, his temperature may thereby be quickly raised or lowered, as the case may be. The daily variation of temperature is present in the fevered patient, but it is irregular, easily

disturbed, and may in some cases show a tendency to inversion of the ordinary curve, which is a rise during the day, the time of activity, and a fall during the night, the time of rest and sleep.

There is a personal equation to be observed both during health and disease; the temperature varies even in the same individual at different stages of life. In infants (4) the regulation is imperfect; in young children the temperature is more easily raised or lowered and a high temperature has not the same serious import which it would have in an adult; in the old and feeble a grave condition of fever may be present with little or no indication of a rise in the internal temperature of the body; on the contrary, there may be a fall in temperature.

The following classification of temperatures is that given by Wunderlich (5), who was one of the first to recognise and teach the great value of the thermometer in the practice of medicine:—

Slight fever 100·4° to 101·12° F. (38°-38·4° C).
Moderate fever 101·3° to 102·2° (38·5°-39°) in the morning, and rising to 103·1° (39·5°) in the evening.
Considerable fever 103·1° (39·5°) in the morning, and 104° (40·5°) in the evening.
High fever 103·1° (39·5°) in the morning, and above 104·9° (40·5°) in the evening.
Hyperpyrexia 107·6° (42°) or more.

Such a classification, however, is purely artificial, and serves little purpose; the actual temperature in degrees and the part of the body in which it was observed are the statements of value, not the interpretation as regards the process of fever, which is implied by the terms slight, considerable, and high. A patient with a high temperature may be in a much less serious condition of fever than another patient with a lower temperature, although both are suffering from the same disease. Indeed, a very low temperature during fever is a bad clinical sign, and is generally evidence of severe toxæmia.

Fever, it would appear, can be correctly considered as a process of disordered metabolism; in most cases it is caused by the invasion of the body by a pathogenetic organism, and thus it comes about that specific organisms, causing as they do special disturbances or diseases, produce types of temperature often peculiar to those diseases. The fever dates from the time of the successful invasion; the rise of temperature may be considered as evidence of the failure of the ordinary resistance of the body. Whether the rise of temperature may or may not be due to a further process of resistance, whether, in short, it may be beneficial or harmful, will be considered later (p. 855). In fever, therefore, there is an *initial stage* during which the temperature rises slowly or rapidly as the case may be. During this period the patient may exhibit the condition known as *rigor*; he looks pale or dusky and cold, he huddles himself together, his teeth chatter, he shivers and shakes, and complains of feeling miserably cold all over his body. Although he is in a fever, and

the internal heat of his body is rising rapidly above the normal, he feels cold; his sensations are based upon the impulses from the sensory nerves of the skin, and the skin, especially of the extremities, *is* cold, is below the normal cutaneous temperature. This cold fit may last half an hour, or perhaps an hour or two. The more marked it is the more rapid is the rise of internal temperature. In other cases the rigor is absent, and the first stage is one of depression and of a feeling of chilliness; the internal temperature gradually rises, the daily variation starting each day from a higher level, until about the fourth day the first stage is merged into the second. The first stage is succeeded by one of warmth, at first agreeable in its contrast to the rigor, but soon to pass into an uncomfortable or intolerable condition of heat. This second stage is the *fastigium*. The disorder is now at its height, the skin is often flushed and hot, and the patient complains of his abnormal heat and thirst. The duration of this stage varies according to the nature of the disease; it may last only a few hours as in ague, or many weeks as in typhoid fever; its severity varies; it is the stage of danger.

The third stage is that of *defervescence*, the return towards the normal. It may begin suddenly and proceed rapidly, as in the so-called *crisis*, the temperature falling two or three degrees Fahrenheit (1° to 1·8° C.), or even seven degrees (4° C.) in seven or eight hours, the patient meanwhile sweating profusely. On the other hand it may occur by *lysis*, the temperature falling gradually, to rise again and then to fall slowly towards the normal in the course of two or three days. During this stage the fall of temperature is in most cases to a point below the normal, the full power of regulation is not regained at once, and during convalescence a rise of temperature may be induced by slight exciting causes, such as mental excitement, food, or muscular effort. In some diseases the fall of temperature is much more gradual, and it is difficult or even impossible to say when the third stage begins.

Pyrexia is not only shown by the abnormal heat of the body, but by changes in temperature and by the nature of the daily variation, the existence of which in health has already been mentioned. The disturbance introduced by fever may be shown in the time or the range of variation, or in both. Should the daily range be slight, as in pneumonia, there is said to be *continuous* fever; if the range be greater, *subcontinuous* fever; and *remittent* if the variation be one degree or more. The term *intermittent* is given to the fever when there are alternating periods of subnormal and high temperature, as in malaria. It is interesting to note that in many cases of fever a rise or fall of temperature is most accentuated at the ordinary time of the maximum or minimum respectively.

Considering, as we may in the case of many diseases, the onset of pyrexia as a sign of the successful invasion of the body by the pathogenetic organism, the fastigium as the continued contest between the tissues and the noxious germs or their poisonous products, and defervescence as the outcome of the successful defence offered by the

tissues, we should expect to find death most frequent during the second stage. The temperature of the dying patient may show an excessive rise or a marked fall; either may indicate serious damage to the nervous control of the temperature of the body. In some cases death is not foreshadowed by any change in the temperature.

Regulation of Temperature in Fever.—Although the temperature of a fevered patient is abnormally high, the nervous control is not absent, it is only impaired; in fact Liebermeister (6) held that the mechanism of regulation resembled that found in the healthy man with this sole difference, that the mean point was "set" at a higher level. This view, however, cannot be accepted, for the characteristic of the fevered patient is the labile state of his nervous control over the heat of his body; his temperature is easily raised or lowered by disturbing conditions which would have little or no effect upon the mean temperature of a healthy man. The feverish patient is easily affected by cold, nervous excitement, and muscular effort. Observations made upon men and animals show that during fever there is little tolerance of heat or cold. Thus it has been found that feverish rabbits and guinea-pigs show a fall in internal temperature if they be placed in a room at 59 to 64·4° F. (15° to 18° C.), but a rise if the temperature of their surroundings be 75·2° to 86° F. (24° to 30° C.). This to a great extent explains the frequent occurrence of low temperatures in animals suffering from fever, for their regulation of temperature is less perfect than that of man. It is necessary to remember that the power of regulation possessed by warm-blooded animals has been evolved (7), not only through the animal series, but even in the individual. A premature infant cannot regulate its temperature, and, unless fostered with artificial heat, becomes colder and colder until death occurs, generally before the rectal temperature is as low as 68° F. (20° C.). Even in the healthy newly-born babe the power of regulation is incomplete. This power appears to depend upon the control exercised by the nervous system upon the muscular system in its widest sense, including voluntary muscles, the heart, and the muscular fibres of the blood-vessels; in addition it entails the control of glandular activity, including, especially in man, the sweat-glands. Of all animals the regulation is the most perfect in man, and associated with his naked condition is the great development of the vasomotor system and sweat-glands. Such a complex nervous power can be disturbed, the delicate adjustments can be overthrown; this is shown in fever by undoubted signs. At one stage of fever there is augmented muscular action, associated with increased production of heat, as seen in the shiverings of rigor; muscular spasm, as shown by the contracted condition of the cutaneous arterioles, which is associated with a diminished loss of heat and a lack of a normal discharge of sweat. At another stage there is marked flushing of the skin, and in some cases profuse sweating. Examination of the exchange of material also gives evidence of disturbance; there is an increased discharge of urea

and other nitrogenous substances in the urine, an abnormal respiratory exchange and disordered glandular activity. It follows, therefore, from the foregoing remarks that in fever the regulation of temperature may be disturbed as regards the production of heat, the loss of heat, or both processes. One factor may be more accentuated in one stage or in one disease, the other factor in another stage or in another disease, and the evidence to be given later will show that no hypothesis of fever is satisfactory which relies only upon the one or the other of these two factors.

A rise in the temperature of the body may be produced by a failure of the regulating mechanism to adjust the loss to the production of heat. It may be due to increased production, diminished loss, or to both of these conditions; further, it may be caused by an augmentation or even by a diminution of both processes, provided that the loss is insufficient to compensate for the production. The increase in the production of heat may be far less than that seen in a healthy man engaged in severe muscular work; the absolute amount is not the important factor. The root of the matter lies in the relation of the production to the loss, in the imperfect regulation of the two processes. The healthy man at work greatly increases his production, and at the same time his loss of heat, so that the one is more or less balanced by the other; it is true that a rise of temperature is seen, but this is probably beneficial, causes little or no discomfort, and quickly subsides when rest is taken. The patient suffering from fever does not so balance his production and loss of heat.

Stress must be laid upon these fundamental points, for there has been an undue tendency to look for an explanation of the high temperature during fever either in an increased production, or in a diminished loss of heat. If it be remembered that both processes are involved, that it is the regulation of temperature which is disordered in fever, then much of the apparent discord in the results of different observers will be seen to be apparent only and not real.

Production of Heat in Fever.—The production of heat during the process of fever has been the subject of many experiments, but the difficulties in the way of exact investigation in the case of man are enormous. It is important that the observations should be made upon man as well as upon animals, for man is characterised by the perfection of his regulation of temperature and the great development of his vasomotor system and sweat-glands, which are associated with the nakedness of his body.

Observations with the thermometer give valuable data concerning the heat of different parts of the body and the daily variations, but the results are not quantitative. It is true that the distribution of the heat of the body can be studied by the determination of the temperature of the mouth, axilla, groin, rectum, and skin, and can be compared with the normal; evidence, however, is wanted upon the loss of heat, which depends not only upon the difference between the temperature

of the body and that of its surroundings, but also upon the evaporation of moisture from the skin and respiratory tract. In some measure the moisture from the skin may be roughly estimated by the increase in the weight of a capsule of calcium chloride applied for a definite time to a portion of the skin (8). In order to obtain exact data the pathologist must use some form of calorimeter and also estimate the exchange of material, such as the intake of food-stuffs and oxygen, and the output of carbon dioxide, water, and nitrogenous waste materials. Liebermeister (9) used a bath as a calorimeter, and calculated the loss and production of heat in a patient in the following manner :—The increase in the temperature of the water multiplied by the volume of the water in litres represents the number of kilo-calories of heat lost by the patient in a given time. If, in addition, the internal temperature of the patient before and after the bath and his weight be known, then his production of heat can be gauged, for the specific heat of the body can be assumed to be about 0·83. This method is chiefly of historical interest. There are many corrections to be applied ; heat is absorbed by the material of which the bath is composed ; there is a loss of heat from the head and neck, from the ventilation of the respiratory tract, and the evaporation of moisture therefrom ; heat is also lost from the bath and water. It is, moreover, very difficult to determine accurately the temperature of a large mass of water, for it forms strata at different temperatures. It is true that the method can be used at the same time as a therapeutic measure, and the results obtained with the fevered patient can be compared with those yielded by a healthy subject or by the patient after convalescence. The environment, however, is unusual, and thus the results cannot be taken as a measure of the production and loss of heat of a patient lying in bed or clothed. By this method Liebermeister found that the production of heat was increased during pyrexia. Leyden (10) was one of the earliest investigators who made observations upon the discharge of heat from fevered patients ; he used a partial calorimeter, which enclosed one limb, and concluded from his results that the loss of heat might be two or three times as great as in the normal subject. Exact results, however, cannot be obtained by such a method. It is necessary to know the loss of heat from the whole body. In this respect the investigation of Langlois (11) is of importance ; infants suffering from broncho-pneumonia were placed in an air-calorimeter devised by Richet, and they showed an increase of 10 to 15 per cent in the production of heat as compared with the afebrile condition.

It is obvious that, if an increase in the loss of heat can be proved and the temperature of the body remains normal or above the normal, there must be an increase in the production. The data must be derived from observations of sufficient duration to eliminate any transient effects, for the mass of the body is so great that time is necessary for a change in the production or loss of heat to produce an effect upon the temperature as observed in some internal parts of the body, and for

the subject to accommodate for his environment. In a healthy man this latency is short owing to the effective control exerted by the nervous system upon the circulation, but in the fevered patient this control has been disturbed. The distribution of heat in the body may be divided into three zones: the internal zone (the viscera), the middle zone which includes most of the muscles, and the outer zone which comprises the skin and subcutaneous tissues. In the first and second regions the temperature is high and fairly constant; in the third it is low and subject to considerable variations; the production of heat occurs almost entirely in the internal and middle zones, the loss of heat chiefly from the outer zone, for the inspired air, even when the external air is cold, is warmed almost to the temperature of the body, and is almost saturated with water before it reaches the larynx. The circulation of the blood tends to equalise the temperature of the body by carrying the warm blood from the internal and middle zones to the vessels of the outer zone. It thus follows that, other conditions being equal, an abundant or meagre supply of blood to the skin will determine a fall or rise respectively in the temperature of the mass of the body. Evidence of an increase in the production of heat, on the other hand, must be sought in the inner and middle zones, in the glandular and muscular sources of heat; during the process of fever such evidence is found in the increased nitrogenous discharge, the increased intake of oxygen and output of carbon dioxide, and during rigor in the shivering and increased tone of the muscles. Therefore, in both health and disease, there is available, in addition to the calorimeter, another method of measuring the production of heat in the body —the estimation of the total respiratory exchange.

The Respiratory Exchange as a Measure of the Production of Heat during Fever.—The oxidation which occurs in the body can be determined by an estimation of the absorption of oxygen and the discharge of carbon dioxide; the results thus obtained are a measure of the heat produced, not an exact one it may be, but still a measurement which compares favourably with the data obtained with the calorimeter.

The values obtained for the respiratory exchange of a fevered patient must be compared, not with those yielded by a normal individual taking food and living an active life, but with those of a healthy man kept in bed and fasting, or at least receiving only a fever-diet, for food and exercise greatly increase the metabolism. The absorption of oxygen rather than the discharge of carbon dioxide affords the basis for the estimation of the processes of combustion, for a meal of carbohydrates will within three or four hours greatly increase the output of carbon dioxide without a corresponding increase in the absorption of oxygen. It is possible, when both the intake of oxygen and the output of carbon dioxide are determined, to calculate not only the quantity, but also the quality of the combustion; from the value of the respiratory quotient, $\frac{CO_2 \text{ vol.}}{O_2 \text{ vol.}}$, conclusions can be drawn as

to the nature of the substances, proteids, carbohydrates, or fats, which are undergoing oxidation.

There is sufficient agreement among the results obtained by different observers to warrant the statement that fever is often, but not necessarily always, accompanied by an increased respiratory exchange. Some of the earliest observers, among whom must be named Liebermeister (12) and Leyden (13), found an increase in the discharge of carbon dioxide, in some patients even as high as 50 per cent of the normal; but they determined only the discharge of carbon dioxide. Later observers, Loewy (14), Langlois (15), Babák (16), and others (17), have in many cases found a definite increase, but it is generally not above 20 per cent of the respiratory exchange in the afebrile condition. Here, again, it is necessary to insist upon the complexity of fever and to point out that the apparently contradictory results obtained with reliable methods by competent observers may be, and probably are, correct. Fever is in many cases accompanied by an increased combustion, but in others the disturbance of the regulation of temperature may be such that the temperature is abnormally high because the loss of heat is so diminished that it is insufficient to balance even a production of heat which is below the normal. These facts are especially demonstrated by the results recently obtained by Babák, who investigated simultaneously by means of a combination of the calorimeter and the respiration-chamber the discharge of heat and the respiratory exchange of children suffering from fever. He found that the decrease in the loss of heat may be so great that the temperature rises even when the oxidation remains at, or slightly below, the normal level; on the other hand, the combustion and production of heat may be so great that even a greatly increased loss does not suffice to prevent the temperature of the body from rising to, and remaining at, an abnormally high level.

Loewy, Speck (18), and others have maintained that the increased respiratory exchange during the febrile process is due to increased muscular activity, and not to the specific febrile process; it is, so to speak, merely an accident. This view, however, is open to serious objections; the shivering, the increased respiratory movements, and the restlessness of a fevered patient are characteristic signs of fever, although they vary with the nature of the disease.

The quality as well as the quantity of the oxidation must be considered. The processes of combustion in the tissues of a feverish patient, who is taking little or no food, show that he is living upon his reserves or even upon his own flesh; the increased nitrogenous waste demonstrated by the greatly augmented discharge of urea proves that proteid substances are chiefly involved. The muscles compose nearly half the weight of the body, and signs of their oxidation are found in the marked wasting which is observed during fever. Indeed, fever must in many aspects be compared with starvation (19); it is often accompanied by partial starvation, and one of the dangers of prolonged

fever is the general failure seen in starved animals. The existence of this nitrogenous destruction is confirmed by the respiratory quotient, the relation of the intake of oxygen to the output of carbon dioxide; the quotient is often low, 0·7, and resembles that of a fasting man. Quotients even as low as 0·5 have been observed by Régnard and Loewy, but their exact significance is a matter of dispute and cannot be adequately discussed here; all that need be stated is that they indicate that the oxidation during the process of fever is different in quality as well as quantity, from the conditions present in the healthy, well-fed man.

Although it is impossible to dogmatise upon the respiratory exchange and production of heat during fever, some data may be useful as examples of what has been found in the human subject.

Observer.	Date.	Temperature of Subject before and after Observations.	Per Kilo. Body-weight and Hour.					Disease.	Remarks.
			Oxygen absorbed in c.c.	Carbon dioxide discharged in c.c.	$\frac{CO_2}{O_2}$	Heat produced in Kilo-calories.	Heat lost in Kilo-calories.		
Babák	Jan. 21	40·5°, 40·5°C.	812	536	0·66	(3·79)	3·79	Broncho-pneumonia	Infant four months old.
,,	,, 28	38·0°, 38·5°	750	534	0·71	(3·88)	3·71	,,	
,,	Feb. 12	37·4°, 37·3°	912	692	0·76	(4·82)	4·79	Convalescence	
,,	March 1	37·4°, 37·3°	712	570	0·80	(4·41)	4·40	Health	

Observer.	Temperature of Subject.	Volume of air breathed per min. in c.c.	Carbon dioxide per cent.	Oxygen per cent. (absorbed).	Carbon dioxide per min. in c.c.	Oxygen per min. in c.c.	$\frac{CO_2}{O_2}$	Nitrogen of urine in grms.	Disease.	Remarks.
Loewy	37·7° C.	7624	2·7	3·7	207	281	0·74	12	Pulmonary phthisis	Man aged 45 years, weight 50 kilos.
,,	40·2°, 39·9°	7937	3·5	3·9	281	316	0·88	17	,,	8½ hours after injection of 8½ mg. of tuberculin.
,,	37·[illegible]	7344	4·1	4·8	303	357	0·85		Early pulmonary phthisis	Man aged 36 years, weight 67 kilos.
,,	40·0°, 40·1°	8237	4·0	4·4	330	365	0·9		,,	8 hours after injection of 3 mg. of tuberculin.

These examples are especially interesting, for they afford a comparison of the respiratory exchange in the same individuals when the temperature at one time was normal, and at another time was high. In the first case given above the respiratory exchange and the loss of heat were less in the condition of pyrexia than in health.

The discussion upon this part of the subject has been confined to the observations made upon man, for not only are these the most important to the physician, but the great development of the vasomotor system,

which distinguishes man from other warm-blooded animals, makes it impossible to draw from the results obtained upon fevered animals conclusions directly applicable to man.

Loss of Heat in Fever.—The heat lost by a healthy adult man in twenty-four hours is about 2500 kilo-calories, of which about 70 per cent are due to radiation and conduction from the skin, 15 per cent to the evaporation of moisture from the skin, 7 per cent to the evaporation from the respiratory tract, and 4 per cent to the expired air, which has been warmed to the temperature of the body. The temperature of the skin is, therefore, most important in connexion with the loss of heat; it can be determined most exactly by the thermo-electric method (21), but results of considerable value can be more readily obtained at the bedside by the use of mercurial thermometers with flat bulbs (22). The highest temperature in health is found over the skin of the abdomen, and is generally between 93·2° and 95·0° F. (34° and 35° C.).

The most important series of observations upon the temperature of the skin in patients with fever was made by Geigel (23); he used the thermo-electric method of Kunkel, and determined the surface-temperature of the forehead, sternum, arm, and leg in cases of phthisis, erysipelas, and typhoid fever. The results show that during the initial stage of fever the surface-temperature is below the normal, the skin is cold; during the fastigium it rises above the normal, and remains raised during defervescence, unless sweating occurs when it falls. Thus there is diminished loss of heat during the stage of rigor, and increased loss during the other stages of fever. The first factor in the production of the fall in the temperature of the body during defervescence is an increased flow of blood to the skin. The temperature of the skin depends upon its vascular condition, which can be studied not only by the thermo-electric method, but also by inspection and the plethysmograph. It has already been shown that during the initial stage of fever the skin is pale owing to the marked constriction of the cutaneous arterioles, and that its temperature is below the normal. Determinations of the variations in the volume of a limb by means of the plethysmograph afford a measure of the alterations in its blood-supply. Observations of this kind made by Maragliano (24) upon patients suffering from fever showed that before the temperature of the body began to rise there was a constriction of the limb, and as the temperature rose this increased until both reached their maxima. A fall in the temperature of the body was accompanied by an increase in the volume of the limb. The results obtained with the calorimeter have already in part been stated in connexion with the production of heat. Langlois investigated by Richet's calorimeter the loss of heat in infants with broncho-pneumonia, and sums up the results as follows:—During the first stage of fever the loss of heat is often below the normal; during the second stage it is increased, but does not show any correlation with the internal temperature; during defervescence it is at its maximum.

Next in importance to the temperature of the skin is the discharge

of sweat. In health sweating is associated with a flushing of the skin with blood, but in fever the relationship is disturbed; often the skin is flushed, but sweating is absent. The condition varies in different diseases, but as a general rule sweating is absent during the rigor and the fastigium, abundant during defervescence. In rheumatic fever and acute miliary tuberculosis sweating is often marked during the fastigium. During the crisis of a fever the temperature begins to fall before sweating appears. In short, it may be stated that the loss of heat by sweating is diminished during the periods of rising and maintained temperature, increased during the period of falling temperature. The loss of heat by the evaporation of moisture from the respiratory tract is increased during pyrexia, for the respiration is more rapid and the temperature of the body is higher. The expired air is also warmed to a higher degree, and is greatly increased in amount in those cases of fever in which the lungs are involved; in these ways more heat is abstracted from the body.

Metabolism.—During fever the marked characteristic of the metabolism or exchange of material is the exaggeration of the katabolic or destructive phase; the respiratory exchange is increased; the destruction of proteid, as shown by the output of nitrogenous substances in the urine, is abnormally great, and there is often much wasting and loss of weight. The increased nitrogenous waste is in part due to the loss of appetite and inanition, for the patient is obliged to draw upon his reserves, and when these are exhausted, to live upon his own tissues Inanition, however, is only a partial cause, for compared with a healthy man upon a similar diet the fevered patient shows a greater destruction of tissue, and loses about 4 per cent more of his body-weight.

It has already been shown that the respiratory exchange is increased in most cases of fever, and it is now necessary to consider the nature of the combustible material. The reserves of carbohydrate, the glycogen of the liver and muscles, quickly disappear during fever in animals. In patients suffering from diabetes sugar is sometimes absent from the urine during an attack of fever, and this event has been brought forward as evidence of increased destruction of carbohydrate. Upon this, however, stress must not be laid, for the fever produces a loss of appetite and inanition, and in many cases, in which attention has been paid to the question of diet, sugar has still been found in the urine of febrile diabetic patients (*vide* p. 859). The fall in the respiratory quotient during the progress of fever indicates that the reserves of carbohydrates are exhausted in the early stages of the disorder. Evidence of the oxidation of fat is found in the disappearance of the deposits of fat which are so characteristic of healthy women and children. At the same time that the reserves of fat in the body are destroyed, it is possible that fat may be formed during the destruction of the proteid of the tissues, for the respiratory quotient is in some cases very low, and a fatty degeneration or infiltration of the tissues, whichever it may be, has been described as a characteristic of prolonged fever. The administration of carbohydrates (25) and fats during fever diminishes the destruction of proteid, and thus

affords confirmation of the utilisation of these food-substances, whether they be given as food or stored in the body before the disease begins.

The difficult question of the destruction of proteid remains. Numerous investigations on the constituents of the urine have been made to elucidate this, but it still remains obscure. Dr. Ringer (26) found that the increase in the output of urea often occurred before the rise of temperature; this, however, is not always the case, and it is necessary to remember that time is required to raise the temperature of the mass of the body, and that observations of the temperature in the mouth or axilla often fail to give the true internal temperature of the body. Several observers, among whom may be mentioned May and Speck, strongly maintain that the rise in the output of nitrogen is secondary to the rise of temperature. It is agreed that the increased nitrogenous output persists during the pyrexia, and for several days after the temperature has fallen below the normal. The destruction of proteid is greater than that seen during inanition unaccompanied by fever, and is different in kind. Albumoses are often present in the urine during fever, and point to an abnormal proteid disintegration. The increase in the uric acid, creatinin, acetone, oxybutyric acid, and volatile fatty acids of the urine is, Speck maintains, characteristic of the disintegration of living tissue under conditions of diminished oxidation. Acetone (28) is not to be considered as characteristic, for it has been found in small quantities in the urine of healthy men and in larger amounts during starvation. What are the causes of this increased proteid destruction? It is generally agreed that there are several; the immediate toxic action of the fever-producing substances upon the protoplasm of the tissues, the condition of inanition, for a fever diet is a starvation diet, and the rise in the temperature of the body. The evidence can only be given briefly. An increase in proteid destruction is seen in the cachexia produced by malignant disease (29), although it is unaccompanied by a rise of temperature; healthy men or animals, when they are fasting (30) or on a fever diet, show an increased nitrogenous waste, for they live upon the proteid of their tissues; healthy men or animals also exhibit an augmented output of nitrogen when their temperature is artificially raised by hot air or baths, and this is even more marked if they have been kept without food for some time before the experiment (31). No one of these factors alone appears sufficient to account for the nitrogenous waste seen during fever. The practical importance of this question is very great, for upon its correct interpretation depends the proper feeding of fevered patients. This subject is discussed elsewhere (*vide* p. 858), and all that need be said here is that food, whether it be proteid, carbohydrate, or fat, will, provided it be assimilated, prevent that part of the waste of the tissues which is due to inanition.

The increased nitrogenous output which is seen after the temperature of the patient has fallen is probably due to the disintegration and elimination of the proteid from those tissues which have been damaged by the toxic substances of the fever-producing organisms or by the high temperature.

It does not appear to be due to recovery from any previous disturbance in the circulation or in the functional power of the kidneys, for analyses of various organs show no evidence of an accumulation of urea in the fevered body; there are no uræmic symptoms, and when urea is given to fevered dogs it is rapidly and completely discharged by the kidneys (32). Speck maintains that the increased waste of the tissues is due partly to diminished oxidation, to a want of a due supply of oxygen contingent upon failure in the circulation, and partly to the effect of the high temperature. He would explain the increased respiratory exchange as entirely due to the increase of muscular activity. Even if this be granted, it would appear more correct to consider the shivering during the rigor and the restlessness of a fevered patient as a part of the disease and not an accident. The influence of toxic substances, apart from a rise of temperature, is shown by the experiments of Krehl and Soetbeer (33), who infected cold-blooded animals with pathogenetic organisms, and caused thereby a marked increase in the production of heat and the output of carbon dioxide, although the temperature of the animals did not rise.

Secretion and Excretion.—The activity of the digestive glands is affected during fever, but it is difficult to analyse the effects, to determine whether they be due to the toxic influence of the fever-producing substance, to the condition of inanition, or to the high temperature. The work of Pawlow (34) and his pupils holds out promise of such an analysis in the future, for by means of the method of isolating a miniature stomach with intact nerves and blood-vessels it has been possible to observe qualitative and quantitative changes in the gastric juice during pathological conditions. At present, however, exact knowledge upon these questions is wanting.

The secretion from the salivary glands is generally much diminished, but the dryness of the tongue cannot be attributed wholly to this cause, for the increased temperature and the breathing through the mouth produce a great loss of moisture. Fever is, moreover, accompanied by a marked loss of appetite, by a failure of that psychical stimulus to the glands of the alimentary canal which has been shown by Pawlow's work to be of the utmost importance. This mental condition may be exhibited as a mere absence of appetite, or by a positive loathing of food; it may be due to a direct toxic effect upon the central nervous system produced by the pathogenetic organisms or their products, or it may in part be due to the high temperature of the body, for the healthy man often experiences a diminished appetite and an increased thirst when he is exposed to hot surroundings. A further factor is introduced by inanition, for the experience of fasting men shows that, after the first pangs of hunger during the first day or two, there is little or no craving for food. Hydrochloric acid is often absent from the gastric juice secreted during fever; if this should be the general condition a good basis for the administration of hydrochloric acid would exist, for the acid is not only of value in gastric digestion, but also indirectly in the production of *secretin*, which

stimulates the pancreas (35). About the activity of the liver little, indeed, is known. Its work may be increased by the nitrogenous waste of the body, but there is no storage of glycogen during fever. The mammary gland is affected, for in nursing mothers the secretion of milk is greatly diminished or ceases during pyrexia.

The condition of the sweat-glands has already been considered in relation to the loss of heat from the skin, but it may be again mentioned that sweating is absent during the rigor and fastigium, but during defervescence is marked and in some cases so profuse that the patient's clothing is drenched. There are, however, differences and exceptions to this general rule; thus in rheumatic fever, septicæmia, and acute miliary tuberculosis the secretion of sweat is often marked during the fastigium. During the crisis of a fever the temperature begins to fall before the sweating is seen. Pilocarpine will cause sweating in a fevered patient, but the effect produced thereby upon the temperature is slight or inappreciable. The disturbance in the activity of these glands would appear to be due not to any alteration in the circulation of the blood, but to the absence of the nervous impulses which in a healthy man are discharged by the central nervous system in response to a general or local rise of temperature. The importance of the nervous system is well shown in cases of traumatic section (36) of the spinal cord in man; sweating is absent in the paralysed portions, and, if the temperature of the body be abnormally high, occurs only upon the unparalysed parts. Pilocarpine, moreover, will in these cases produce a secretion of sweat only in those parts of the skin which are unaffected by the paraplegia.

The work of the kidneys is gauged by the quality and quantity of the urinary constituents (37) in relation to the intake of food and water, but it is necessary to discriminate between the changes which are due to the kidney itself and those abnormalities which during fever arise from the disorder of metabolism. The correlation between the sweat-glands and the kidneys is well known, and in fever appears to be maintained, and thus will in part account for variations in the quantity of urine. During the period of incubation and the rigor there is often diuresis, caused, it may be, by a rise of blood-pressure due to the constriction of the cutaneous arterioles as well as by the diminished loss of moisture from the skin. With the progress of the fever the urine is diminished, for there is increased loss of water by the lungs, and in many cases by insensible perspiration; the intake of fluids is, moreover, often below that required by a healthy man. When the temperature falls there is often copious diuresis which may persist for a day or two; during this time, as has already been shown, there is an increased nitrogenous output. The specific gravity of the urine generally varies inversely as the quantity. Upon this question of the output of water there has been considerable discussion; some observers have maintained that there is a retention of water, and that the tissues become more watery, although no signs of œdema may be present. It is possible that the loss of water does not at all times correspond with the loss of solids, but at the crisis

the balance will be adjusted or turned by the profuse sweating. In prolonged and severe fevers the loss of vasomotor tone and the failure of the circulation is often associated with œdema of the internal organs and a failure in the excretion by the kidneys.

In connexion with the hypothesis of a retention of water it is necessary to discuss the *excretion of chlorides.* The interesting observation that during fever the urine may become almost or quite free from chlorides has attracted much attention from clinical observers, and several hypotheses have been propounded to explain it. A deficiency in the chlorides of the food taken by a fevered patient was one of the earliest explanations, but it was not accepted. By some authors it was maintained that the chlorides were not filtered through the kidney owing to retention in the exudates or excretion by other channels, especially the bowels; by others it was held that the chlorides filtered through the renal glomeruli, but were reabsorbed. The vitalists, on the other hand, insisted that the kidney excreted no salts when the proportion of salt in the blood fell below a certain amount which was necessary for the activities of the body. The whole question has been recently investigated by Sollmann (39), and his conclusion is that the disappearance of the chlorides from the urine during fever is due entirely to the deficiency in the intake of the salt in the food. He finds that the composition of the febrile urine corresponds in this respect almost precisely with that of the urine of a healthy man placed upon a diet poor in chlorides—the characters of a fever diet. The body apparently requires a certain amount of sodium chloride for its metabolic processes, and retains it when the supply is deficient. Sollmann, in a joint research with Hatcher (40), also investigated the condition during typhoid fever in two patients whose urine was almost devoid of chlorides. The results show that the disappearance of the chlorides is not responsible for any great change in the other urinary constituents. The addition of sodium chloride to a milk diet increases the excretion of urine and of metabolic products, and on this account Hatcher and Sollmann think that the addition of salt to the amount of fifteen grammes per day to milk is to be recommended in the treatment of fever.

The increase in the urea, uric acid, ammonia, sulphates, and phosphates of the urine is to be attributed to the increased proteid disintegration, and not to any change in the renal function. The ammonia is said to be increased to two or three times the normal amount, and to be related to the neutralisation of the acids formed during the proteid destruction, but since a similar increase is found in the urine of healthy subjects who are taking in food poor in nitrogen, it cannot be considered as peculiar to fever. Even at the risk of repetition it must be insisted that fever is a condition of inanition.

The increase of urinary pigments has been urged as evidence of an abnormal destruction of red blood-corpuscles. The albumoses often present in febrile urine are probably derived from the abnormal proteid destruction in the body, whereas the albumin appears to be due to the

direct toxic effect exerted by the pathogenetic organisms or their products upon the kidneys, as in the case of scarlet fever and diphtheria. A very high temperature of the body and circulatory disturbances are also factors in the causation of febrile albuminuria. The polyuria of Bright's disease does not disappear during fever, whereas diabetic polyuria does; an explanation for this is found in the origin of the former in renal disease and the diuretic action of sugar in the latter; fever does not improve the condition of the kidney, but may greatly influence the metabolism of sugar either directly or by the concomitant inanition.

It is interesting to note, as evidence that fever may affect the synthetic power of the kidney, that in fevered herbivorous animals benzoic acid does not combine with glycocoll to form hippuric acid. It is impossible, however, to discuss the difficult question of the chemistry of febrile urine adequately in a short general article; references, therefore, are given to special treatises upon the subject (41).

Respiration.—The respiratory exchange has already been discussed, but attention must be drawn to the effect of fever upon the respiratory movements. They are increased in number, even apart from any disease of the lungs or other portions of the respiratory tract; they may be shallow or deep, and thus the total ventilation will vary; no exact investigations, however, appear to have been made upon this latter point. The probable cause of the rapid respiration is the high temperature of the body, for experimentally the rhythm can be increased by warming the blood which supplies the respiratory centre in the medulla oblongata (42); and in dogs, as Richet (43) has shown, the respirations may be enormously increased by exposure to heat. Moreover, in the crisis of pneumonia the rate of respiration falls with the temperature at a time when the condition of the lungs is probably but little changed as regards the area of consolidation. Other factors, such as the effects of the carbon dioxide in the blood, and the direct effect of toxic substances upon the respiratory centre, have so far not been investigated. It is true that the amount of carbon dioxide in the arterial blood in cases of fever, unaccompanied by disease of the lungs, is said to be below the normal, but this gives no index of the pressure of the carbon dioxide in the blood or tissues of the nervous system, and this, as Drs. Haldane and Priestley (44) have shown, is the factor which determines the frequency of respiration. The breathing may also be increased as a part of an effort of compensation in cardiac cases; the respiratory movements exert a pumping action upon the blood, and assist the right side of the heart to maintain a proper supply of blood to the lungs and the left side of the heart.

Circulation.—In health the circulation of the blood is generally influenced by changes in the beat of the heart or the condition of the blood-vessels; in fever several sources of disturbance are introduced, some direct, such as the high temperature and toxic substances, others indirect and due to defective nervous control. Additional factors are found in the abnormal metabolism, the condition of inanition, and the

frequent respiration. The complexity is thus very great, and here it will only be possible to indicate the influence of these various factors.

The effect of a rise of temperature is seen in an increased rate of heart-beat; this, as is well known, can be easily demonstrated upon the organ whether it be isolated or intact within the living body. Liebermeister taught that the rate of the pulse and the temperature followed parallel lines, and that a rise of 1° C. (1·5° F.) was accompanied by an increase of eight beats. This is by no means a general rule, for it has been shown above that the heart is influenced by other factors besides the high temperature. The heart does indeed appear to be very susceptible to a rise in the temperature of the body, and in heat-stroke cardiac complications are frequent. It is difficult, however, to decide in such cases whether the cardiac affection is secondary or not, for men with "weak" hearts are especially liable to be overcome by muscular exertion in hot and damp surroundings; the regulation of temperature under unfavourable conditions makes an additional demand upon the circulation.

The cardiac failure which may occur in diphtheria appears to be due to the toxic action of the bacterial products upon the cardiac muscle; some observers have maintained that the cardiac nerves are also affected. It is uncertain how far the rapidity of the heart-beat may be due to lack of nervous control exerted through the cardiac nerves.

The control of the diameter of the arterioles is maintained by the vasomotor centres, and during fever there is evidence of their abnormal condition; during the rigor the skin is pale owing to the powerful contraction of the arterioles, due to impulses through the vaso-constrictor nerves; during the fastigium this tone is largely lost, and the vessels become dilated and liable to variations in calibre from time to time. The abnormal condition is shown by the observation that if the finger-nail be drawn across the skin of a feverish patient the resulting pallor persists for a considerable time. The flush on the cheeks of phthisical patients, and on the cheek of the same side as a unilateral pneumonia, is also evidence of vasomotor disturbance. It is probable that the splanchnic region is also involved, and should the loss of tone be marked the effect of the dilatation of this extensive area of vessels upon the pressure and flow of blood will be proportionately great; the pressure will fall and the flow of blood will become sluggish, although the more rapid contraction of the heart may to a certain extent counteract this. Thus even with widely dilated cutaneous vessels the loss of heat may be inadequate owing to the diminished velocity of the blood. In debilitated or aged subjects hypostatic engorgement is frequently seen during fever.

The condition of inanition of a patient with fever is also a cause of cardiac weakness, for even in healthy men during prolonged fasting the response of the heart during muscular exercise is inadequate; its muscle-fibres appear to lack reserves of combustible material, and cardiac failure or dilatation may result.

From all these combined effects it is obvious that the weakening of the heart in prolonged fever may become so great as to produce fatal

results. In this connexion it should be pointed out that the good effects of the treatment of fevers, especially typhoid fever, by cold water may in considerable measure be due to the effect upon the circulation; the improved tone of the vessels and of the heart-beat would appear in many cases to be largely responsible for the mitigation of the nervous symptoms.

The pressure of the arterial blood is generally raised during the rigor and early days of a fever, when the cutaneous arterioles are constricted and the heart is beating more frequently; later the pressure falls and is often associated with a well-marked dicrotic pulse, for the tone of the blood-vessels and the cardiac contractions have become weaker.

In connexion with the circulation a few remarks may be made about the blood. During fever the percentage of hæmoglobin and the number of red corpuscles show a decrease, but the total quantity present in the body may or may not be altered, for no accurate determinations of the volume of the blood appear to have been made upon fevered patients. The carbon dioxide in arterial blood is stated to show a decrease during fever, and this has been attributed to a decrease in the alkalinity of the blood arising from an increased production of acid during the abnormal proteid metabolism; upon these points, however, further investigations are greatly needed (Leucocytosis, *vide* pp. 683, 850).

Nervous System.—The master-tissue of the body is the nervous system, and its condition during fever has attracted much attention, for several of the best-known hypotheses of fever have been based upon nervous disturbances, either over-activity, diminished activity, or partial paralysis. These views have been greatly strengthened by the observation that lesions of the central nervous system or the action of drugs thereon will produce hyperthermia. In the first place, therefore, it will be well to consider the evidence of nervous disturbance in fever, and then in the concluding part of this article to examine those cases of hyperthermia which can be produced at the will of the experimenter by direct action upon the nervous system of healthy animals. An examination of such cases cannot fail to throw light upon the nature of fever, although it must be prefaced that such cases of high temperature are not examples of fever in the strict sense of the term.

Incidentally attention has already been drawn to many of the signs of disturbance of the nervous system during fever. The sensory effects are shown in depression, loss of appetite, and those unpleasant but familiar sensations which are so difficult to analyse or describe, but are expressed by the term "feeling unwell." Delirium is common, and it is noteworthy that it may only appear in the evening, at the time when the temperature is generally higher, and there is, even in the healthy subject, a tendency for the mind to wander during sleep and to dream. The motor effects are exhibited in restless, or in some cases even convulsive movements. The influence upon the vasomotor centres is well-marked; at first excitation, associated with constricted cutaneous arterioles during the rigor, then diminished activity and instability, due

it may be to fatigue, or the prolonged action of the toxic agents, and shown by the dilatation of the blood-vessels and their lack of tone; an increase, however, in the discharge of vaso-dilator impulses may occur, especially at the crisis. The chief characteristic of the nervous system during fever appears to be a decrease in stability and co-ordinating power. The nervous regulation of temperature is present, but is disordered and imperfect; proof of this has already been given in contrasting the effects of cold baths, excitement, and food upon healthy and fevered subjects, and additional evidence is found in the marked influence exerted upon fevered patients by doses of antipyretics which would have little or no effect upon healthy men. Shivering is an evidence of the outflow of nervous impulses; the healthy man shivers when he feels cold, so does the feverish patient; by muscular movement both increase their production of carbon dioxide and heat, but the latter discharges in addition an increased quantity of nitrogen in his urine. The shivering in each case appears to be a response to the cooling of the sensory nerve-endings produced by the marked constriction of the cutaneous arterioles, for external heat will often abolish it; the feverish patient is under no delusion when he says that he feels cold, for it has been shown that his skin is indeed cold even at the time when his internal temperature is abnormally high. It must, however, be mentioned that nervous excitement may cause shivering movements.

The disturbance of the nervous system is undoubted, but to explain how it is caused is very difficult owing to the complexity of the febrile process; here it is only possible to indicate the various factors which appear to be responsible (*vide* p. 846). Foremost must be placed the direct toxic action of pathogenetic organisms, their products or substances produced by abnormal changes in the tissues, for the nervous symptoms are often antecedent, and out of proportion, to the rise of temperature. A toxin or a drug (45) may by its action upon the nervous system produce opposite results according to the dose which is administered; in small doses a rise, in large ones a fall in temperature and collapse, and thus the effects may be excitatory, paralysing, or both in varying degrees; this is important in its bearing upon the gravity of some cases of fever in which the temperature is low. Krehl and Matthes (46) found that tuberculin in small doses will cause a rise, in large doses a marked fall in temperature and collapse.

As the next important factor in the production of the nervous effects may be given the high temperature, for in heat-stroke it is often very marked, and is most successfully relieved by the application of cold. Failure or lack of adjustment of the circulation must also be remembered as another factor.

Theory of Fever.—A historical account of the theories of fever has been given by Sir John Burdon-Sanderson in the introduction to this article, and it only remains to consider in relation thereto the bearing of the rise of temperature which can be produced in animals by various experimental methods. Many observers have investigated the disturb-

ances in temperature which result from injury of various portions of the central nervous system. Section of the spinal cord in the cervical region will, as Pflüger (47) clearly demonstrated, deprive a warm-blooded animal of its capacity to maintain its temperature; it now resembles a cold-blooded animal, and its exchange of material and temperature largely depends upon the temperature of its surroundings; there may thus be normal, subnormal, or very high temperatures. Such a condition obtains in man after traumatic section of the spinal cord (36), but those cases in which the temperature is high cannot be properly described as fever or pyrexia in the strict sense of the terms, but should be known as hyperthermia.

Puncture of various parts of the brain, especially in the region of the corpus striatum and optic thalamus, will cause a rise of temperature or hyperthermia, and this has been urged as evidence of the nervous origin of fever. The general result (45) of the numerous investigations upon this subject is that the rise of temperature is due to increased production, associated at first with diminished loss of heat. The increased combustion occurs in the liver and muscles; there is an increased output of nitrogen, but this appears to be a result, not a cause, of the high temperature, for it follows and does not precede the increased heat, is inconstant, and small in amount in comparison with that seen in fever. This puncture of the brain disturbs the co-ordination of the central nervous system, upon which the control of the temperature of the body depends; the disorder, however, arises apparently not from stimulation or injury of any special "heat centres," but from a transient disturbance; it may be either augmentor or inhibitory in effect, to the flow of incoming and outgoing nervous impulses, which are concerned in the co-ordination of the various organs of the body, especially the muscular system in its widest sense. This hyperthermia cannot be produced in anæsthetised animals, or in animals whose reserves of glycogen have been exhausted by previous starvation or excessive muscular exercise. Albumoses are not discharged in the urine of an animal the temperature of which has been raised by puncture.

It is well known that a rise of temperature may be produced by exposure to high temperatures; some of the symptoms resemble those of pyrexia, and there is an increase in the output of nitrogen, but no albumosuria. Heat-stroke (48) is a condition of hyperthermia, not of pyrexia, if we use the latter term in the sense of a febrile rise of temperature, for there is no evidence in support of the view that heat-stroke is an infective disease.

Some drugs and animal and vegetable extracts cause a rise of temperature by their influence upon the nervous system; the condition thus produced should also be known as hyperthermia. Fever is something more than a condition of hyperthermia; it is not an entity, but a convenient clinical term for a group of phenomena with a more or less definite sequence and origin. In the first place, it appears to be a disturbance of metabolism due to the effect of pathogenetic organisms

or their products; the toxins affect all the tissues at the same time that they may show a special action on one organ. In the case of the central nervous system, the first stimulating effect would seem to be indicated by the discharge of impulses down the vaso-constrictor nerves, which, by the production of pallor of the skin, would give rise to a sensation of cold, and thus indirectly to the shivering of rigor. The diminished loss of heat and the increased production would raise the temperature, and the response would be increased metabolism, which can no longer be controlled by the disordered nervous system. The natural course of the progress of fever would depend upon compensation by the production of anti-bodies or other methods of antagonism, and thus might be explained the different course run by febrile diseases due to specific organisms. This direct relation of attacks of pyrexia to specific organisms is well seen in malaria and relapsing fever. *Thus fever may be defined as a response in metabolism to the invasion of micro-organisms and a toxic disturbance of the nervous regulation of temperature.* The critical question, whether a real condition of fever can arise without such an invasion, is discussed in connexion with hysterical fever, catheter fever, fever in association with gall-stones, hæmorrhage, and other conditions (*vide* p. 849).

If fever be a response of the organism to the invasion of pathogenetic organisms, the question arises whether the high temperature may be beneficial, harmful, or indifferent in its effect upon the resistance offered by the infected subject. Opinion has been divided between the extreme views; according to the ancient view, fever is beneficial, a purification from the disease by means of heat; the high temperature enables the animal to oxidise, antagonise, or destroy the injurious organisms or their products. A more modern school would look upon the high temperature as the enemy chiefly responsible for the evil effects produced by a fever, and on that account to be combated by cold and antipyretics. Upon philosophical and experimental grounds the old view is again receiving more and more support; bacteriological investigations (49) show that high temperatures (39° to 40° C.) arrest or attenuate the growth and virulence of many micro-organisms, and experiments (50) upon animals show that a high temperature enables them to resist more successfully the effects of pathogenetic organisms. These views and their influence upon the treatment of fever are discussed elsewhere (*vide* p. 855). From a physiological point of view the high temperature would appear only to be harmful when it is of such a height or so prolonged as in itself to endanger life.

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M. S. P.

CLINICAL CONSIDERATIONS AND TREATMENT

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Causes of Fever.—We know that the cause of fever in many diseases is a micro-organism, or poisons manufactured by it, and in many others, *e.g.* measles, the fever so closely resembles that of diseases undoubtedly due to micro-organisms that we may safely assume that micro-organisms are the cause here also. Some other poisons may cause a rise of temperature, but it is doubtful whether the term fever should be applied to such pyrexia. Thus a marked rise may occur in belladonna

poisoning, the temperature reaching 104° F. Strychnine and caffeine may also raise the temperature a little, but the most remarkable drug in this respect is β-tetrahydronaphthylamine (1), which may raise a rabbit's temperature 10° F. in less than two hours. On the other hand large doses of alcohol will depress the temperature. As has already been mentioned, it is possible in animals to cause a rise of temperature by experimental damage to the central nervous system, notably if the part damaged is the corpus striatum (2). This is of special interest as bearing on cases in ordinary practice in which pyrexia is due to injury of the central nervous system. It is an old observation that a tumour, softening, or hæmorrhage in the pons will lead to considerable pyrexia, which may also follow damage to one crus or to the upper part of the spinal cord. When pyrexia is induced by a lesion in the cerebrum the damage is usually in the corpus striatum or its immediate neighbourhood. Next most often the motor area of the cortex is the seat of the damage; thus the blood-clot due to a middle meningeal hæmorrhage will, by its pressure on the cortex, cause a rise of temperature to 109° F.; but there is hardly any part of the brain a lesion of which has not at some time or another caused a rise of temperature. Seeing, however, that disease of the cord, of the pons, of one crus, of the basal ganglia, and of the motor area of the cortex will all cause pyrexia, it is highly probable that in man the course of at least some of the nervous impulses which control the temperature is the same as, or much the same as that of motor impulses. It is true that disease of other parts of the brain will cause pyrexia—thus we have known hyperpyrexia to be due to a cerebellar tumour; but it must be remembered that sometimes a tumour or other lesion of the brain is found at the autopsy to be in a position different from that indicated by the symptoms during life (4); nor is this surprising, for it is easily conceivable that the balance may be so upset by, for example, a new growth within the cranial cavity that parts far removed from the lesion may be exposed to pressure or suffer from interference with their vascular supply. In the case of cerebellar tumour just mentioned, in which the temperature reached 107·4° F., the corpora quadrigemina and surrounding parts were much compressed by the tumour.

Usually the duration of pyrexia dependent upon damage to the brain of man is short, and this is also true of that produced experimentally. No doubt when disease of the brain is due to micro-organisms, *e.g.* meningitis or cerebral abscess, pyrexia is due partly to absorbed toxins acting on the thermic mechanism generally, and partly to direct affection of the brain. This is borne out by the extreme irregularity of the temperature in many diseases of the brain; for example, it is more irregular in tuberculous or streptococcal meningitis than in tuberculous or streptococcal disease in which the meninges or brain are not affected. Thus in one case of meningitis the temperature varied between 96° and 106° F. in a few hours. Direct damage to the brain by injury often causes a very high temperature; for example, it is

observed in cases of middle meningeal hæmorrhage, lacerated brain, and fractured skull. Many cases in point have been collected. Some of the functional diseases of the nervous system illustrate the importance of disturbance of it in producing pyrexia; thus it is no uncommon thing to observe some pyrexia after an epileptic fit and in delirium tremens. When this is slight it is possible that the overaction of the muscles in these diseases may have had something to do with the pyrexia, but not infrequently the rise of temperature is so great that we are forced to assume that functional disturbance of the nervous system has played some part in the rise of temperature. For example, a child recently under my care had a series of epileptic fits, and the axillary temperature rose to 107·4° F. Dr. T. Oliver gives a case in which a temperature of 109° F. was reached, and a rise is seen in the status epilepticus. Among 129 cases of delirium tremens collected by Fiüs there was a rise of temperature in 91 per cent. Hyperpyrexia is not very rare in this disease, and I have seen the temperature reach 108°. Many writers mention pyrexia occurring in chorea, and in one case in Guy's Hospital the temperature was 108·4°; but chorea does not illustrate the influence of the nervous system on the temperature so well as epilepsy or delirium tremens. I have carefully read most of the recorded cases of hysterical pyrexia, and although some are examples of fraud on the part of the patient, in others there seems no doubt that the pyrexia was genuine. When we remember the wide range of symptoms in hysteria, it is not surprising that pyrexia may be one of them. The importance of the nervous system in relation to pyrexia is well illustrated by the frequency of hyperpyrexia in connexion with disease of the brain and cord. Dr. J. H. Bryant collected from the records of Guy's Hospital 100 cases of hyperpyrexia—that is, in which the temperature exceeded 106° F. Twenty-nine, or nearly one-third, were examples of lesions of the brain or cord, three were examples of delirium tremens; of these thirty-two cases thirty-one were fatal, but the mortality of hyperpyrexia, apart from disease of the brain, is only 77 per cent. The difficulty of reducing the temperature in some of these cases of nervous hyperpyrexia is great, prolonged immersion in cold water being necessary to effect a reduction.

As has just been shown, the most common lesion in the central nervous system to cause pyrexia is one of the corpus striatum. The pyrexia presents some peculiarities which render it worthy of consideration. The lesion is almost always hæmorrhage from one of those branches of the middle cerebral artery which pass through the anterior perforated space. Not all hæmorrhages in this situation produce pyrexia; sometimes the damage is too small, sometimes the hæmorrhage is so profuse that the fall of temperature caused by loss of blood and shock is not counteracted by the damage to the corpus striatum; but usually the fall below normal only lasts a few hours, the temperature then rises to one, two, or three degrees above normal, the maximum being usually reached in about twenty-four hours; the temperature then slowly falls,

the normal point being reached in a few days, after this it usually falls a degree or so below normal, and remains subnormal for a few days before attaining the healthy standard. The temperature, whether above or below normal, is often for about a week after the hæmorrhage higher in the axilla of the paralysed side than in the axilla on the same side as the lesion. At first the excess may amount to a degree, gradually it becomes less. I attempted to discover the cause of this by taking the surface-temperature, and at the same time estimating the amount of sweat secreted on each arm. It is clear that the arm with the higher surface-temperature or secreting the greater amount of sweat will be losing heat the faster of the two arms. By this method it was found that the loss of heat was greater from the arm of the paralysed side, that is to say, the side on which the axillary temperature was higher. But the axillary temperature is an internal temperature, and the loss of heat is therefore greater on the side on which the internal temperature is higher. This being so, more heat must be produced in paralysed than in the healthy muscles. These observations (8), if confirmed, suggest that as the muscles are the chief thermogenetic tissues, a lesion which paralyses their motor function exalts their thermogenetic activity.

Certain clinical examples of pyrexia suggest that damage to other parts of the body may cause a rise of temperature such as that associated with gall-stones, with the passage of a catheter, and that following severe burns. Some have thought that the rise of temperature which follows the passage of a catheter or the passage of gall-stones is always due to the absorption of bacterial products through some abrasion of surface of the urethra or bile passages, others consider that the rise of temperature is due to the severe peripheral stimulus acting on some part of the central nervous system that has to do with the maintenance of a constant temperature; in the same way some hold that a similar explanation meets the case of the rise of temperature which follows a simple fracture, others think that this is due to the absorption of blood and damaged tissue from the site of injury, or to bacteria which develop in the effused blood. In this connexion it is interesting to remember that a very high temperature may follow a severe burn. Thus, in the paper referred to above, Dr. J. H. Bryant records six cases in which temperatures of 109·8°, 108°, 107·2°, 106·4°, 108°, and 106·2° F. were reached. It is true that septic absorption from the burnt part may have been the cause of this pyrexia, but it is equally true that such a severe peripheral stimulus as a burn may have reflexly affected the central nervous system so as to cause pyrexia.

In other diseases—*e.g.* pernicious anæmia, splenomedullary leukæmia, and exophthalmic goitre, no explanation of the pyrexia has yet been discovered; probably it is toxic, the fever-producing agent resulting directly from the disease; in this connexion it is interesting to note Chittenden's (9) suggestion that in certain fevers "incomplete products of tissue-metabolism are important factors in the production of febrile temperatures."

Symptoms.—So little work has been done on the subject of fever in comparison to its complexity that we are much in the dark about its fundamental symptoms. We hardly know, for example, in any given fever how far many symptoms are the direct result of toxæmia, and how far they are merely dependent upon the pyrexia. The increased rapidity of the pulse is undoubtedly partly due to the pyrexia, but often the rate of the pulse is modified by the fever-producing agent, as, for example, in typhoid fever and influenza, in which it may be slow even when the temperature is raised. The rapidity of respiration associated with pyrexia is by no means in all cases solely the result of the rise of temperature; for example, in lobar pneumonia the respirations are rapid and out of all proportion to the temperature, and this increased rapidity is not due to the area of lung involved, for it diminishes greatly in a few hours after the crisis. Albuminuria is in some instances probably the direct result of the pyrexia, but it is so much more frequent in diphtheria and scarlet fever than in other fevers that it must to a great extent be due to some special action of the toxins of these fevers. In the same way leucocytosis, although so often associated with pyrexia, should not be regarded as dependent upon pyrexia, for it is absent in enteric fever, influenza, malaria, measles, German measles, and tuberculosis. A furred tongue and delirium are both commonly associated with pyrexia, but inasmuch as the character of the furring and the frequency of delirium vary in different fevers, neither of these phenomena can be ascribed solely to pyrexia. Enough has been said to show the extreme complexity of the subject, and it is clear that the greatest caution must be exercised in ascribing any symptom in a fevered patient solely to pyrexia; indeed, strictly speaking, there is no exact clinical picture which can be given as indicating fever generally, for the character of fever differs in different diseases. But although it is impossible to give an accurately detailed description applicable to all fevers, a broad outline can be depicted and the symptoms which compose this have been already discussed (*vide* pp. 826, 842).

The onset of the pyrexia varies in different fevers; thus pneumonia and malaria are nearly always ushered in by a rigor, while in other fevers, such as enteric, rigors are very rare, and it is noteworthy that in children rigors are quite exceptional. As a general rule, a rigor is associated with a rapid rise of temperature, *e.g.* in pneumonia, malaria, and pyæmia; nor is this surprising, since the constriction of the cutaneous vessels and the rapid succession of muscular contractions entail diminished loss and increased production of heat. But a rapid rise of temperature frequently occurs without any rigor, for example, in rheumatic hyperpyrexia, and rigors are rare in those cases in which a high temperature is due to disease of the nervous system.

Mode of Production of Pyrexia in Man.—In some fevers pyrexia is due chiefly to a diminution in the loss of heat, in others chiefly to an increased production. It would be satisfactory to be in a position to say of any given fever (*e.g.* measles) that the pyrexia is mainly

dependent on one of these two factors, but this, in the present state of our knowledge, is impossible, and it is quite conceivable that at one period of the same fever the pyrexia might be due principally to diminished loss of heat, and at another principally to an increased production. Theoretically the best method of settling this question would consist in observations with a calorimeter, but the fallacies of the instrument are usually so great that the results must be received with great caution, and, further, it is almost impracticable to put a fevered patient into a calorimeter. The available observations on this point and the attempt to solve the question by means of observing the respiratory exchange have been mentioned above (*vide* p. 830). The simplest clinical method of attacking the problem is to observe simultaneously the internal temperature, the surface temperature, and the amount of sweat secreted. By inverting on the skin of the patient a glass box filled with calcium chloride, and weighing it before and after inversion, the amount of sweat can be estimated. If elevation of the surface-temperature and the increase in the amount of sweat secreted are associated with a raised internal temperature, it is clear that the production of heat must be increased, for although the internal temperature is raised, the loss of heat by both radiation and evaporation is greater. The following table is abstracted from more complete tables (8) :—

Case.	Date.	Mouth Temperature.	Abdominal Surface Temperature.	Mouth-exceeded Surface-Temperature by	Excess of Mouth during Fever.	Excess of Surface during Fever.	During Fever Surface rose more or less than Mouth.	Milligrammes of Sweat from given area of Abdomen in Ten Minutes.	Greater or less Sweat in Fever in Milligrammes.
Enteric fever . I.	June 9	102·0	95·0	7·0	...	...	...	0·7	...
,, ,, . ,,	July 2	98·2	92·0	6·2	3·8	3·0	−0·8	2·1	−1·4
,, ,, . II.	June 9	102·0	97·8	4·2	...	...	...	1·1	...
,, ,, . ,,	July 2	98·0	93·2	4·8	4·0	4·6	+0·6	1·3	−0·2
,, ,, . III.	Oct. 23	103·0	96·0	7·0	...	...	...	...	...
,, ,, . ,,	Nov. 3	99·4	94·8	4·6	3·6	1·2	−2·4	3·0	−3·0
,, ,, . IV.	Oct. 22	103·0	97·2	5·8	...	...	...	1·4	...
,, ,, . ,,	Nov. 3	98·8	95·2	3·6	4·2	2·0	−2·2	7·2	−5·8
,, ,, . V.	Dec. 3	104·0	93·2	10·8	...	...	...	1·0	...
,, ,, . ,,	Dec. 11	98·4	91·4	7·0	5·6	1·8	−3·8	3·0	−2·0
Lobar pneumonia I.	Mar. 6	104·2	97·6	6·6	...	...	...	1·8	...
,, ,, . ,,	Mar. 10	99·6	92·6	7·0	4·6	5·0	+0·4	2·4	−0·6
,, ,, . II.	Apl. 30	103·6	97·8	5·8	...	...	...	4·1	...
,, ,, . ,,	May 7	98·8	93·0	5·8	4·8	4·8	...	5·9	−1·8
,, ,, . III.	July 11	103·8	96·8	7·0	...	...	...	2·1	...
,, ,, . ,,	July 20	98·0	95·0	3·0	5·8	1·8	−4·0	5·6	−3·5
,, ,, . IV.	Nov. 29	102·8	96·0	6·8	...	...	...	2·2	...
,, ,, . ,,	Dec. 11	98·0	93·0	5·0	4·8	3·0	−1·8	5·5	−3·3
,, ,, . V.	Dec. 10	104·0	100·4	3·6	...	...	...	3·5	...
,, ,, . ,,	Dec. 17	98·0	92·2	5·8	6·0	8·2	+2·2	5·0	−1·5

With regard to enteric fever, the table shows that in all cases the amount of sweat secreted during the fever was small (from 2 to 3 milligrammes in ten minutes is the usual amount my calcium boxes absorb from the abdomen of a healthy man), and less than when the temperature had fallen; therefore, during the fever, the loss of heat from evaporation was diminished. Also, in every case except one the surface-temperature rose less than the internal—in other words, the loss from radiation and conduction was not increased proportionally to the rise of internal temperature, and was, therefore, relatively to the internal temperature, less during the fever. There is thus distinct evidence that in enteric fever the loss of heat is, relatively to the rise of temperature, diminished, and this diminished loss no doubt helps to raise the internal temperature. Still, as the surface temperature always rises considerably, the actual loss by radiation and conduction must have increased during the fever, and probably the diminished secretion of sweat was not enough to counteract this. We may therefore conclude that although the pyrexia in enteric fever is largely due to a lessened loss of heat, the production is probably increased as well. With regard to pneumonia, all the cases except the first show that the excessive sweating associated with the crisis continues for some days, for in each case the final observation, which is the one here recorded, was made some days after the crisis. This sweating must assist in keeping down the temperature after the fever. In every case the secretion of sweat during the fever is less than when the temperature has fallen, but since the secretion during the fever is still rather more than in healthy individuals and in enteric fever patients whose temperature has fallen, it is probable that the amount of sweat secreted during the fever is usually more than before the fever began. Diminution in the loss of the heat, due to diminution in the secretion of sweat, therefore, probably plays no part in raising the temperature. In only two cases did the surface temperature rise less than the internal, and in two it rose more (thus corresponding with the hot skin of pneumonia); it follows, therefore, that in pneumonia the loss of heat by radiation and conduction during the fever must often be enormous. Since the loss of heat is so increased the rise of temperature is for the most part due to an increased production of heat.

Similar observations showed that, in two cases of erysipelas the rise of temperature was due to an increased production of heat, and that in two cases of suppuration the rise of temperature was due, in part at least, to a diminution in the loss of heat. Many observations were made upon cases of tuberculosis; but it is so difficult to fix a normal standard for these patients that the results are hard to interpret. The outcome of all these bedside observations is that the cause of the pyrexia in fever is sometimes an increased production of heat, sometimes a diminished loss, and sometimes both. Fever, indeed, is to a large extent a different process in different diseases. The advantage of this method is its simplicity; the disadvantage is that it is only

qualitative, and that there must be a certain error, for it is unlikely that the secretion of sweat or the dilatation of the cutaneous vessels is equal all over the body. To a certain extent the condition of the external air will affect these factors; the temperature and movement of the atmosphere, however, remain pretty constant in a hospital ward.

The prognosis of fever can hardly be discussed in general terms; the bearing of the temperature will be considered presently; probably, unless hyperpyrexia is reached, or nearly attained, the temperature itself is not harmful, but since, like leucocytosis, it is the result of two factors, viz. the intensity of the infection and the ability of the body to react to the infection, much experience is needed to gauge its value. Hyperpyrexia is, however, of serious import, as shown by Dr. J. H. Bryant's statistics that the mortality of 100 cases of hyperpyrexia in various diseases was 84 per cent. External temperature certainly influences hyperpyrexia, for 20 per cent of the cases occurred during August, and 51 per cent in the four months June to September. In 59 per cent of all the cases, or in 70·2 per cent of the fatal cases, the hyperpyrexia occurred only during the last few hours of life. The following table is of interest as showing the diseases in which we may expect to meet with hyperpyrexia:—

TABLE *showing the Incidence and Fatality of Hyperpyrexia in* 100 *Cases.*

	No. of Cases.	Deaths.
Acute Rheumatism	7	4
Enteric Fever	6	3
Erysipelas	1	1
Tetanus	2	2
Pyæmia	17	15
Broncho-pneumonia	4	4
Lobar Pneumonia	5	3
Infective Endocarditis	3	3
Tuberculosis	2	2
Ascending Nephritis	4	2
Malignant Disease	4	4
Scalds and Burns	6	5
Brain Lesions	22	22
Spinal Cord Lesions	7	6
Delirium Tremens	3	3
Heat Stroke	2	1
Miscellaneous	5	4
	100	84

In most cases of fever the cause of death is not pyrexia, but the action of the poison of the disease upon the heart, and the outlook is best gauged by the state of the pulse. A dry brown tongue means that the patient is very ill, and patients who sink into the

condition known as the "typhoid" state usually die. While many delirious patients recover, yet, other things being equal, the delirious patient is more ill than one who is not. Children bear fevers much better than their elders, and old people are particularly bad subjects; lobar pneumonia is a good example in point, for children nearly always recover, old people nearly always die. Very fat people bear fever badly, and so do hard drinkers. We often see that it adds very seriously to the gravity of a febrile illness if the patient has kept up and about while the fever was on him. Patients with severe diabetes do not bear fever well. The effect of fever on the excretion of sugar will be discussed presently (see p. 859).

The effect of the incidence of a fever during pregnancy varies; for while pregnancy does not increase the maternal mortality in cases of enteric fever, I think, from many cases I have watched, that if a woman is acutely ill with phthisis, pregnancy leads to an increased activity of the disease, which often proves fatal a few weeks after her confinement. Women with active phthisis should not become pregnant, but if the disease is quite quiescent, they may, and often do, go through pregnancy without any increase in the disease, especially if they are in good circumstances and can lead an out-door existence. Occasionally, however, in such cases the fever becomes active again after pregnancy. Probably mere fever does not matter much to the fœtus, its temperature must rise and fall with that of the mother. The effect of a maternal fever upon the fœtus depends entirely upon whether the infection passes through the placenta. It is extremely difficult for tubercle bacilli to pass through the human placenta. The evidence is undoubted on this point. Not only is the placenta itself excessively rarely affected with tuberculosis, but there are only about half a dozen cases on record in which tubercles have been found in the fœtus of tuberculous mothers, and in such cases, as might be expected, the tubercles are most evident in the liver. Hence, even when the mother herself dies of phthisis at the end of pregnancy, the child is usually alive. It is quite different with typhoid fever, for if the mother has this disease typhoid bacilli may be found in the fœtal blood, which gives an agglutination reaction, not only when bacilli are present in it, but in some cases in which they are not. A collection of cases by Drs. French and Hicks shows this. Hence the mother almost invariably miscarries, and the child is born dead or dies shortly after birth. The evidence goes to show that it takes some days for the bacilli to infect the fœtus; therefore, if the child is viable and the mother has typhoid fever, premature labour ought probably to be induced as soon as possible. On the other hand, if the mother has phthisis, it is usually wise to allow labour to come on naturally. If a child is born while the mother has measles, the disease is present in the child and of the same date as in the mother.

Post-mortem Appearances.—The changes seen after death in any case of fever are so interwoven with those due to the particular cause of the fever, that it is doubtful whether any distinction can be drawn.

The cells of the tissues, especially the muscles and glands, are often cloudy, somewhat swollen, and appear to have undergone parenchymatous degeneration. The heart may be dilated, and this has been ascribed to degeneration of the cardiac muscle. The spleen is frequently enlarged and soft, the blood may be imperfectly coagulated, and sometimes post-mortem staining of the heart and large arteries is very marked.

Meaning of Fever.—As has been pointed out, pyrexia in man is nearly always the result of infection by micro-organisms, and usually some chemical body produced by them is the cause of the rise of temperature. The height attained depends, therefore, upon two factors, the dose of the poison and the power of the thermic mechanism to react to the dose. There is good reason to believe that the rise of temperature, like leucocytosis and the production of antitoxin, is beneficial to the infected patient, provided of course that the temperature is not so high as to be dangerous in itself, that is to say, somewhere about 105° or 106° F.; a patient with such a temperature will always be especially liable to die, for the very height of his temperature indicates that he has a powerful dose of toxin, and such a high temperature is in itself dangerous to life. The view here put forward is *a priori* probable, for a high temperature is fatal to all micro-organisms, but even extreme cold is not. If it were possible for the human body to be heated without damage to a temperature of about 112° F., or a little more, all tubercle bacilli in it would be destroyed, and tuberculosis might be banished from the human race. But there is also direct evidence in favour of regarding pyrexia as a protective mechanism against bacteria, or, in other words, as an attempt at self-sterilisation. In 1880 Pasteur made his classical observation, that fowls which are ordinarily refractive against anthrax bacilli succumbed to them if their temperature had been lowered by cold, and many experiments have since been performed with different micro-organisms and different animals, all showing that pathogenetic bacteria more easily influence animals artificially cooled. Indeed, we are led to wonder whether the comparative harmlessness to man of some infections is not due to his natural temperature. For example, the gonococcus flourishes best between 91° and 98° F., and higher temperatures arrest its development. May it not be that in this lies the explanation of the fact, that although so many thousands of human beings are every year infected by gonorrhœa, yet in so few is the disease dangerous to life. Loewy and Richter even claim that animals whose temperature is raised by puncture of the corpus striatum resist bacterial invasion better than others. Clinically also there is strong evidence that fever is a protective mechanism. A streptococcal infection is a common termination of various chronic maladies, but although this infection does not usually lead to much pyrexia, it is fatal, and possibly one reason for this is that the body-temperature produced by it is not high enough. If a large number of cases of lobar pneumonia are grouped according to the height of the temperature, it will be found

that—provided they do not approach hyperpyrexia—the prognosis is good in proportion as the temperature is high. It is interesting to remember that, speaking generally, the outlook in this disease is good in proportion as the leucocytosis is considerable. The same relationship between prognosis and temperature is seen in bronchopneumonia; for example Holt, analysing the cases in the New York Infant Asylum, found that if the temperature was 106° F. or over, the mortality was 85·5 per cent, when it was between 105° and 106° F. the mortality was 60 per cent, between 104° and 105° F. it was 49 per cent, between 102° and 104° 60 per cent, and when it never reached 102° it was 71 per cent. Excluding the cases in which the very height of the temperature probably helped to kill, we see that the lower the temperature the worse the prognosis. I have frequently observed that if the temperature is low—about 100° or 101° F.—in pneumonia the outlook is bad. It must not be supposed that the paucity of evidence that fever is a protective mechanism militates against this view, for as height of temperature is, other things being equal, proportionate to the virulence of infection, pyrexia might well be a protective mechanism, and yet we might be unable to find any evidence of this. Again, it must be borne in mind that no analysis of cases can bring out in a sufficiently strong light the harmfulness of a low temperature—if it be harmful—for cases with a low temperature include a large number in which the temperature is low because the infection is slight. This is particularly true of enteric fever. It is not to be urged against this view that beneficial treatment frequently reduces temperature, for in the instances most familiar to us it does so because it acts deleteriously on the cause of the disease, and hence the temperature falls; thus quinine is a poison to the micro-organisms of malaria, and so when it is given the temperature falls; diphtheric antitoxin neutralises the poison which causes the symptoms of diphtheria, and hence causes a fall of temperature; all recent work points to the fact that salicylates—which reduce the temperature in rheumatic fever—act directly on the cause of the disease. The benefit following the treatment of enteric fever by the external application of cold water is apparently adverse to the view that pyrexia is a protective mechanism, but probably it is not really so. It has already been pointed out that some of the benefits of cold baths in this fever may be due to their tonic action on the vessels. Again, the reduction in the mortality claimed by the advocates of this treatment is only 6 or 8 per cent, and it may well be that some of the cases saved are those in which the temperature is approaching hyperpyrexia, or perhaps the application of cold acts for good by some other action than that on the vessels or temperature, for example, it has been said that it favours the excretion of typhoid toxins by the urine. Then, too, the statement that the mortality is reduced by 6 or 8 per cent begs the question whether some of the patients may not have been killed by the treatment—possibly by reducing their temperature when it had not reached a dangerous point—for if more cases among those with approaching

hyperpyrexia were saved than were killed among others by the treatment in really unsuitable cases, the net result would be a diminution in mortality. These considerations make it probable that it is better not to put every patient whose temperature attains a fixed point—usually somewhere between 102·4° and 103·4° F.—into cold baths, as is done in some institutions, but to select for cold bathing the cases in which the temperature appears to be harmful. This has the further advantage that we are not blindly treating a mere symptom.

Treatment.—It would be out of place in this article to describe separately the treatment of each febrile disease, but there are a few general principles applicable to all varieties of fever. If the temperature in itself is dangerous, or if, in other words, hyperpyrexia is attained, the patient should be put into a bath. The temperature of this may be about 80° F., and cold water may be gradually added till the water is cooled to 70°; but some prefer a bath of about 90°, gradually cooled to 70°. The exact temperature of the bath will depend upon the apprehension of the patient, his temperature, and the rate at which it is rising. He should be kept in till the rectal temperature has fallen to 100°, and usually this is in about 15 or 20 minutes. He should then be put back to bed and dried, a blanket may be thrown over him, and if there are any signs of collapse a little brandy and some hot-water bottles may be required. He should be carried to and from the bath with a sheet lightly thrown over him, which may for the sake of decency remain across the bath while the patient is in it. If no cold water has been added to the bath, it will be found that the water has been warmed by the heated patient. Cold sponging will usually suffice for children. If a bath is not available, blocks may be put under the head of the bed, and a large macintosh sheet under the patient; this should be banked up at the sides and cold water should be poured into the head end, and the water allowed to run into a pail at the foot of the bed.

Unless the temperature is dangerously high it should not be lowered by artificial means, for clinical experience has shown that the outlook in fevers is not improved by so doing; secondly, we have seen that the probabilities are that fever is an attempt on the part of the body to protect itself against bacterial infection; and, thirdly, the drugs which are powerful antipyretics, *e.g.* antipyrin, acetanilide, and phenacetin are all of them poisonous drugs which depress the heart; it is probable that when they were in vogue many deaths were due to their use. It might be thought that if the rise of temperature is a protective mechanism it would be a good thing to raise it artificially, but if this were done the point of dangerous hyperpyrexia would often be quickly reached, and also the drugs which raise the temperature are all powerful poisons, *e.g.* cocaine, belladonna, and β-tetrahydronaphthalamine. We have already alluded to the striking action of this last drug.

The patient with fever should be in bed. The reasons for this are many. In the first place he usually feels too tired to be up and about. If the rise of temperature is even partly due to an increased production

of heat, several calories of energy must be expended in raising the temperature of the whole of the human body three or four degrees Fahrenheit, as its specific heat is only a little below that of water, therefore less energy will remain for the exertion of walking about. Secondly, if we are right in believing that fever is a protective mechanism, it is a good thing to keep the patient wrapped up by the warm bedclothes and thus prevent loss of heat. On the other hand, as is well known, when there is any danger of hyperpyrexia, loss of heat should be facilitated by getting rid of all bedclothes except a sheet. The importance of going to bed when feverish is very great. Every physician to a large hospital must have noticed how seriously the gravity of fever, *e.g.* typhoid or pneumonia, is increased if the patient has been up and about for some days after the illness attacked him. Although it is not known why badly ventilated, "stuffy" rooms are depressing and disagreeable, the sick-room should be well ventilated. This is best done by widely open windows; if necessary a fire should be lighted, for the temperature of the sick-room should be about 65° or 70° F. A big room is desirable, for the larger the room the less the chance of draught.

If the fever is at all severe, milk is the best food. A milk diet entails much fluid, and this is desirable, as most feverish patients are thirsty, and their salivary secretion is scanty; if they are very ill, they swallow with difficulty, and milk is easy to swallow; and, lastly, their digestion is impaired and milk is easily digested, if in any case it is not, it can be predigested, and if the patient objects to the mawkish taste, the addition of a very little coffee overcomes this. It has been suggested that a milk diet, in virtue of the contained calcium salts, contributes to the occurrence of venous thrombosis in typhoid. This, however, is very doubtful, and the incidence of thrombosis in typhoid is not sufficiently high to outweigh the advantages of a milk diet. Often the thirst is so great that barley-water or some other bland drink is desirable with the milk. Before the time of Dr. Todd, who "fed fevers," many patients were lost owing to the lowering treatment of fever which had been in vogue for many centuries. But sometimes even now fever patients are not fed enough, as is evident from the extreme wasting that follows a prolonged fever. The potential energy of the food of an average man who keeps well, is up and about, but does not take much exercise, should be about 2500 calories. It is impossible to estimate the amount of potential energy which the food of a fevered patient should contain, for although he will need less because he is at rest, he will require more because his temperature is raised, and it is impossible that in any fever this is entirely due to a diminution in the loss of heat, indeed we have brought forward evidence for believing that in some the rise of temperature is undoubtedly due to an increased production of heat. In addition the increased rate of respiration and of the beat of the heart mean an increased expenditure of energy. Unfortunately the amount of food a fevered patient can take is often limited by what he can be persuaded

to swallow, and by what he can digest and absorb, but inasmuch as an average weight for a man is about 66 kilos, every rise of 1° C. in his temperature by increased heat production alone will mean an expenditure of about 55 calories of energy, and probably a man of average weight will require approximately 2000 calories of energy a day if he has a fever and lies in bed. Three pints of milk, the usual amount of milk given daily to a fevered patient, yields only 975 calories. Thus we see that ordinary fever diet is really a starvation diet, hence if the fever is long continued, as in typhoid fever, additional energy must be supplied; this can be best done by adding sugar, which is most readily digested and absorbed. A patient may take four or six dessert-spoonfuls of maltine daily, each of these contain 60 calories, so he will gain from 240-360 calories; or he may take an equal amount of honey, for it is cheaper, and each dessert-spoonful of it is worth 70 calories; or he may have some of the carbohydrate patent foods, but they entail the necessity of the conversion by the patient of their starch into sugar. The best carbohydrate for fever patients is lactose, 2 ozs. may be dissolved in water and added to each pint of milk. Taking an ounce as 30 grammes, and the caloric value of 1 gramme of sugar as 4, the value of each pint of milk after the addition of 2 ozs. of lactose will be increased by 240 calories, or 720 calories for the 3 pints of milk. The administration of additional carbohydrate has this further advantage. It has been shown experimentally that if carbohydrates are given to an animal with fever there is a very great saving in the destruction of fat and proteid tissues, which is of great importance, since the destruction of proteids in fever is very great. In other words, fever without carbohydrates in the food is like raising the temperature of a house by burning it down, but fever with carbohydrates corresponds to raising the temperature of the house by burning coals in the grate. Supposing a patient is taking 3 pints of milk = 975 calories, with 2 ounces of lactose in each pint = 720 calories, the total is 1695 calories, which is almost enough, but the addition of a little cream to each pint brings the amount nearer still to the required 2000 calories, and improves the taste of the milk. Cream should not be substituted for the lactose, as fevered patients digest fat with difficulty, and fat is not a sparer of proteid to nearly the same extent as sugar. Nor should we attempt to make up for the heavy loss of proteid in fever by giving much proteid, for in fever proteids are difficult to digest and absorb, and the body is already so flooded with the products of proteid disintegration that it is unwise to put any more of them into the circulation. Additional interest is lent to the administration of sugar in fever by the observation that the secretion of sugar in the urine in diabetes is often influenced by fever. Usually the urinary sugar is diminished as the temperature rises, but it may be unaltered or even increased. These changes occur without any alterations in diet. The glycosuria produced by excision of the pancreas is diminished by fever, but the pyrexia caused by damage to the brain increases the glycosuria produced by adrenalin, while fever caused by

bacterial infection diminishes it. Richter suggests that temperature alone increases glycosuria, but that the direct effect of the bacteria in bacterial infection is to diminish it. The effect of pyrexia may perhaps be different in diabetes and alimentary glycosuria.

Much judgment is required to give alcohol properly in fever. Many persons at the present time take so little when well that it is disagreeable to them when ill, but it may be useful to induce sleep, and small quantities may improve the appetite. It is chiefly given for its action on the heart; sometimes it slows the pulse and strengthens the beat of the heart of a feverish patient, but more often it has the reverse effect, and, unfortunately, it is impossible to tell beforehand which effect it will have, hence digitalis and strychnine are usually preferable as cardiac tonics. Brandy is generally prescribed when alcohol is ordered for this purpose, and clinical experience shows that very old brandies are more efficacious than newer spirits. A great advantage of alcohol in fever is that it is a food; an ounce of pure alcohol has an energy value of about 200 calories, and the body can utilise this. Further, it is a food which does not require digestion, is easily absorbed, and it is to some extent a sparer of fat. Although it dilates the cutaneous vessels, there is no exact evidence that it lowers the temperature in fever. It may, on the whole, be said that alcohol is often unnecessary in fever, since energy, stimulation of the heart, and the effect on digestion, and sleep may all be obtained by other means; when in any given case it does exert its beneficial effects and the patient feels better for it, 4 or 6 ounces of brandy is the quantity that should be given in the 24 hours, as this amount contributes 400 or 500 calories to the available energy of the food. Lastly, it should be remembered that there are few things in which persons vary more than in their susceptibility to alcohol,—a dose that would be harmful to one by paralysing the activity of the nerve- and muscle-cells of his body will be beneficial to another.

It is well known that beef-tea, meat extracts and juices, provide very little energy, and therefore are not important as foods, indeed some of them are hardly foods at all. Their use in any quantity is undesirable, they distend the stomach and flood the blood with extractives that are passed out by the kidneys, which already have enough to do to excrete the concentrated febrile urine, loaded with the products of the increased and altered metabolism of fever; further, large amounts of extractives are apt to cause diarrhœa. Any good that follows beef-tea and meat extracts is due to their pleasant flavour and their stimulating action on digestion. If at any time it is thought desirable to give a feverish patient additional proteid, it is best done by giving somatose or some other meat powder containing large quantities of peptones, but with this, too, there is a risk of diarrhœa.

No special drugs are desirable for fever, but individual symptoms may require treatment; thus failure of the pulse may be treated with strychnine, given subcutaneously or in a mixture when it may be combined with digitalis. Sleeplessness may be treated with morphine,

chloralamide, trional, veronal, or similar drugs. A little hydrochloric acid often aids digestion, and a simple aperient, as castor oil, is frequently necessary.

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DIVISION II

INFECTIONS

THE INFECTIONS

Of Established Bacteriology.

Septicæmia and Pyæmia.
Erysipelas.
Infective Endocarditis.
Cerebrospinal Fever.
Influenza.
Diphtheria.
Tetanus.
Enteric Fever.
Relapsing Fever.

[End of Volume I.]

Pneumonia.[1]
Anthrax.
Glanders.

Of Chronic Course.

Tuberculosis.
Syphilis.
Actinomycosis.
Leprosy.[2]

Of Doubtful Nature.

Measles.
German Measles.
Scarlet Fever.
Rheumatic Fever.
Chicken-pox.
Small-pox.
Cow-pox.
Mumps.
Whooping Cough.
Typhus.
Glandular Fever.
Foot and Mouth Disease.
Rabies.

Tropical Infections.

Malaria.
Blackwater Fever.
Malta Fever.
Yellow Fever.
Dengue.
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Beri-beri.
Epidemic Dropsy.
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Dysentery.
Hill Diarrhœa.
Sprue.
Liver Abscess.
Leprosy.
Yaws.
Verruga.
Oriental Sore.
Ulcerating Granuloma of the Pudenda.

[1] See Volume V.
[2] Removed to Volume on Tropical Diseases.

SEPTICÆMIA AND PYÆMIA

By W. Watson Cheyne, C.B., F.R.S.

Introduction.—Under this general heading are usually included three constitutional affections which, both pathologically and etiologically, are quite distinct. Speaking broadly, it may be said that they are due to the entrance into the general system either of micro-organisms or of their products; and as a rule they are met with in connexion with some wound or breach of surface, the discharges from which have become contaminated with bacteria. Three different results may follow the entrance of bacteria into a wound, and it is not uncommon to find two or more of them in combination; indeed, in the great majority of cases the condition of sapræmia accompanies that of septicæmia or pyæmia.

The first of these affections is *sapræmia*, which is also spoken of as septic intoxication. Sapræmia is a general constitutional disorder exclusively due to chemical poisoning by the products of bacteria, and not to the entrance of the bacteria themselves into the blood. The poison so introduced cannot increase in the system except by the absorption of fresh doses; and the blood of an animal that has died of the disease only contains a diluted solution of the amount of poison it had received, so that small quantities of this blood, when injected into another animal equally susceptible, will not set up symptoms of poisoning. Hence the disease is in no sense an infective one; moreover, the poison absorbed is being so constantly and rapidly eliminated from the system that, provided the dose already taken up be not a fatal one and that all further supplies are stopped, the disease will of itself come to a spontaneous and favourable termination.

The second form of septic disease, *septicæmia*, or septic infection, is a disorder caused not only by the absorption of poisons from a wound, but also by the entrance of living micro-organisms into the body and their growth and multiplication therein. Although in this case, as in sapræmia, it is probable that the constitutional effects are due solely to the chemical poisons produced by the organisms, and not to the presence of the organisms themselves in the blood-stream, yet there is this cardinal difference, that in septicæmia the poison is being continually produced inside the body; whereas in sapræmia the poison is produced in the wound—that is to say, outside the body—and is absorbed from that part. Hence it generally happens in the case of septicæmia—in contra-distinction to sapræmia—that, if the disease be firmly established, it cannot be moderated by the removal of the original source of infection.

Thirdly, we have to consider *pyæmia*, an acute, general, infective disease, due to the entrance of living pyogenetic micro-organisms into the blood, and especially characterised by the formation of abscesses in

various organs and parts of the body. Here we have not only poisoning of the body with the products of micro-organisms which have already established themselves in the living body, but we have in addition the occurrence of septic emboli, either the result of suppurative phlebitis or thrombosis, or formed in other ways which will be afterwards discussed; these give rise to the abscesses characteristic of the disease.

By some authors a second form of pyæmia is spoken of under the term *Chronic Pyæmia.* This is a disease which arises also in connexion with wounds, which is caused by pyogenetic organisms, and, like pyæmia proper, is characterised by the formation of local abscesses in various parts of the body. These abscesses, however, are fewer in number than in true pyæmia; they chiefly occur in subcutaneous tissues or joints, and apparently they are not due to embolism. For my own part, I prefer to designate this disease by the name "Multiple Abscesses"; for, except that it is due to pyogenetic organisms, it differs widely from pyæmia in its pathology, and should not, in my opinion, be described as a variety of this disease.

So much for definition; but, while for this purpose they are described as quite distinct from each other, it must be confessed that in practice it is not always easy—even at the post-mortem table—to assign definitely its exact part to each of the three forms in the production of symptoms; for, as I have said, two or more of them very often concur. The sharp separation between the three forms depends more on the results of the experiments on animals than on clinical observation; it may be interesting, therefore, to refer shortly to the experiments which have established the pathology of these affections.

Sapræmia.—At the beginning of the last century Albert von Haller, Gaspard, and many others, injected infusions of putrefying meat and other putrid animal fluids into animals, and observed the poisonous effects. They did not, however, attempt to determine the particular constituents on which these effects depended, and Panum was really the first who thoroughly studied this side of the subject. He showed that the poisonous properties of putrid solutions were unaltered by boiling, which would of course destroy all living elements; further, he found that the poison was in solution in the material, and he was able to separate substances in the form of a powder from putrefying materials which produced all the symptoms that occurred when the raw material was employed. This was done in the first place by filtering the fluid, and then adding absolute alcohol until a precipitate was obtained. This precipitate was collected and further purified by repeatedly dissolving it in distilled water and reprecipitating it. Finally, it was dried at a temperature of 100° Centigrade. Even this treatment by alcohol, heat, and drying did not destroy the poisonous products, 0·012 gramme of the powder so prepared being sufficient to kill a large dog.

Selmi attempted to carry the investigation farther in order to determine the nature of the substances present in this powder; and he described a number of different substances, or more probably groups of substances, which he had isolated from putrefying animal tissues. To

these substances, some of which were harmless and some intensely poisonous, he gave the name of animal alkaloids or ptomaines, these substances being transitional products formed by the breaking up of the highly complex organic molecule on its way to form simple inorganic substances. Brieger has also thoroughly investigated this subject, and has isolated and named a number of these ptomaines, such as putrescin, cadaverin, neurin, etc. The organisms which produce these substances are not as a rule pathogenetic, that is to say, they are not as a rule able to live in the animal body. In cases in the lower animals (and also in man) where this intense poisoning has resulted, the organisms are not necessarily present in the blood during life, unless, indeed, the condition of sapræmia be complicated with some infective condition such as septicæmia.

When a quantity of putrefying material is injected into an animal —say a dog—in sufficient quantities to kill the animal, the most prominent symptoms are fever, vomiting, and diarrhœa: great restlessness and muscular twitchings may occur at first, but are soon followed by loss of muscular power; the diarrhœa becomes profuse, serous, and frequently blood-stained, and is accompanied by much pain and tenesmus; the temperature falls, and usually becomes subnormal; the respiratory movements become very feeble; the pupils are dilated; there is marked cyanosis, and death ensues, apparently from cardiac failure. A fatal result usually takes place within twenty-four hours, depending directly on the dose injected and on the size and susceptibility of the animal. Koch describes the symptoms in mice as follows:—"The animal becomes restless, running about constantly, but showing great weakness and uncertainty in all its movements. It refuses food, respiration becomes irregular and slow, and death takes place in four to eight hours." When a smaller dose is employed the effects are similar but less severe, and the animal after a few hours rapidly recovers.

On post-mortem examination in these fatal cases we find no very prominent characteristics. Rigor mortis is transient and slightly marked; decomposition sets in early; there is no inflammation of the tissues in the neighbourhood of the site of injection. The chief changes occur in the blood, which is dark in colour, coagulates slightly and very imperfectly, and stains the lining wall of the veins and endocardium. Occasionally serous effusions are met with in some of the serous cavities, and these are also blood-stained. Small, dark extravasations of blood are also commonly seen beneath the skin and serous membranes, and occasionally elsewhere throughout the body; the spleen is greatly swollen, often pulpy and dark, from engorgement with blood; there may be signs of severe gastro-enteritis with intense inflammation of the mucous membrane of the stomach and intestines, and with partial or almost complete desquamation of the epithelial lining (Burdon-Sanderson). Microscopical examination of the blood shows that the red corpuscles tend to form clumps instead of the usual rouleaux; it is found also that the staining of the vessel-walls depends partly, at least, on hæmolysis and the presence of hæmoglobin in the blood-plasma.

Septicæmia.—Koch, in confirmation of Panum's experiments, found that if a considerable quantity of putrefying blood were injected into animals, poisoning of the animals advancing to a fatal result was brought about; the blood of the animals so killed did not contain any bacteria, and was not capable of transmitting the disease. He further found that the rapidity and severity of the result were proportionate to the amount of putrid material injected; but when small quantities (one or two minims) of putrid blood were injected into mice, although no immediate symptoms were produced, yet in about one-third of the cases evidence of disease appeared within twenty-four hours, and if so a fatal result usually ensued. The same events also took place where much smaller doses were employed, but in this case the proportion of animals affected was still less.

The symptoms so set up were as follows:—After about twenty-four hours greatly increased conjunctival secretion came on, which appeared to glaze the eye, and ultimately glued the lids together; the animal soon ceased to eat, appeared overcome with lassitude, and moved but little; soon it sat still with its back bent and its legs drawn up; the respiratory movements were slow and feeble; the weakness increased, and death slowly ensued in forty to sixty hours. On post-mortem examination there was slight œdema at the site of the injection; the spleen was considerably enlarged, but no other marked changes were found except in the blood. Under a high power of the microscope numerous extremely minute bacilli were found in the blood, some free, others filling up the white corpuscles. The minutest quantity of this blood inoculated into a healthy mouse led to the disease, which was therefore a true infective one. Koch was subsequently able to cultivate these organisms, and the disease resulted from the inoculation of the cultivated organisms in the same way as from the inoculation of the blood.

Since this time a number of organisms have been found which produce similar symptoms in various classes of the lower animals; thus, in the case of rabbits, at least three different kinds of organisms set up these symptoms. This disease in the lower animals is spoken of as septicæmia, and is looked upon as the counterpart of septicæmia in man; but, in human septicæmia, as will be presently pointed out, organisms cannot be demonstrated in the blood in numbers at all comparable to those in the lower animals, or indeed in sufficient numbers to account for the disease, supposing it to be a simple blood infection.

Pyæmia.—In the course of Koch's researches on mice and rabbits he came across an organism which produced a condition in these animals comparable to pyæmia in man; and he found that this condition was due to the development of micrococci in the blood. It differed from human pyæmia in not being associated with thrombosis and embolism of portions of the thrombus, but similar plugs were formed in the vessels in another way, which is also of interest in connexion with human pyæmia wherein it is possible that something similar may take place. He found that this organism grew in the blood, and formed

colonies in which masses of red blood-corpuscles became incorporated; in this way emboli were formed which stuck in the smaller vessels. Another way in which a similar result was produced was that the organisms seemed to attach themselves to the endothelial cells, and, growing there, ultimately filled up the lumen of the blood-vessel and formed a plug. It is possible that a similar thing may occur in man, more especially in connexion with the streptococcus pyogenes. Numerous experiments have also been made to determine the part which embolism plays in the production of pyæmia, but I may leave the reference to these until we come to speak of the pathology of pyæmia in man.

The clinical characters of these diseases as met with in practice must next be briefly described.

They may occur in connexion with surgical operations, injuries, or diseases. Pure acute sapræmia, as above defined, is rarely found in surgical practice, and can only occur in the case of large wounds or cavities, such as the peritoneum, which are imperfectly drained; but it probably is not uncommonly seen in a milder form, and plays a part in the traumatic fever which so usually accompanies a septic wound. *Hectic fever* may be either a chronic sapræmia or a chronic septicæmia; that is to say, it is a state in which small doses of septic poison are constantly being absorbed either from the wound or from the tissues in which the organisms are situated. Septicæmia may result from wounds of any size, even from mere scratches if they happen to be infected with the necessary organisms of sufficient virulence. Pyæmia may also result from wounds of any kind, or from surgical diseases associated with suppuration. Usually thrombosis occurs in the veins leading from the affected part, and the emboli resulting from the breaking down of the thrombus lodge in the first capillaries at which they arrive; consequently in most cases, where the systemic veins are affected, the lungs are the chief, or, it may be, the only part attacked. Pyæmia following acute osteomyelitis is of the same type and due to the same causes; and although commonly described as a distinct variety of the disease it presents no special characteristics. The same may be said of the rarer cases occurring in connexion with cellulitis, local abscesses, etc.

Puerperal fever, again, can no longer be considered as a separate disease. The uterus after parturition or abortion presents a large raw surface exactly comparable to that of a recent wound; and any of the forms of septic disease, or any admixture of them, may arise as the result of the retention of decomposing materials in its cavity, or of infection of the discharges. It may, however, be here noted that in these cases there is a special liability to the retention of a large mass of putrefying material in contact with a large absorbing surface, so that pure sapræmia is more often found in this than under any other conditions.

Ulcerative, infective, or malignant endocarditis may occur in the course of an ordinary pyæmia, or may appear to be the starting-point of the disorder. In either case the pathological picture is peculiar, in that the primary affection occurs, in the great majority of cases, in the left

side of the heart; thus the emboli given off from it lodge in the systemic arteries or capillaries and lead to a true arterial pyæmia (Wilks). Beyond this, and the fact that the emboli are usually in great abundance, and that the lungs are not affected in the first instance, this disease does not differ from ordinary pyæmia [*vide* art. "Infective Endocarditis"].

Suppurative Pylephlebitis is a true pyæmia, where the original site of infection is situated somewhere in the area drained by the portal system of veins. It is then in the radicles of these veins that thrombosis occurs; and the resulting emboli will lodge, in the first instance, in the portal veins or capillaries of the liver. It may, in short, be accurately described as portal pyæmia [*vide* art. "Pylephlebitis," vol. iv.]. A rare form of this disease is occasionally seen in the newly born, and is sometimes described as umbilical pyæmia. It results from suppurative phlebitis of the unobliterated umbilical vein.

Idiopathic or spontaneous pyæmia and septicæmia are names applied to those cases which present the ordinary clinical features and post-mortem appearances of this disease, but in which the source of the infection cannot be discovered. These cases will be further discussed later, but it may be here remarked that most of the published cases seem to be examples of multiple abscesses rather than of true pyæmia.

Infective myositis, an exceedingly rare disease characterised by multiple abscesses in the muscles throughout the body, has also been classed under pyæmia, but its pathology has not as yet been properly worked out.

A. Sapræmia

Etiology in Man.—The following conditions may be taken as necessary factors in the production of this disease in man: (1) There must be a large mass of dead material, whether injured tissues, blood-clot, or exudation, which is undergoing putrefactive changes; (2) this putrefying material must be in contact with a large, rapidly absorbing surface such as would be furnished by a fresh wound, a serous surface, or the like; (3) tension in the wound, keeping the discharges under pressure, and mechanically aiding their absorption.

It may also be accepted that the poisons will produce greater effects, or, conversely, that a smaller dose will be required, in persons who are debilitated, who are at either extreme of life, or in whom the excretory functions, which play so important a part in the elimination of the poison, are in any way impaired.

These demands will be satisfied by such conditions as the following:—After parturition or abortion, portions of placenta, membranes, or blood-clot, if retained in the uterus, are very apt to become infected with putrefactive organisms and to undergo rapid decomposition. The interior of the uterus furnishes a large, raw, rapidly absorbing surface, so that a large dose of the poison must be absorbed. In many cases, also, the patient may be suffering from a certain amount of physical

exhaustion or mental distress which renders her more susceptible to the poisonous influence. In surgical practice it may be met with after severe injuries, when a large, deep wound contains gangrenous tissue, blood, or discharges undergoing decomposition; also after operations when large cavities are left, as after the removal of large tumours, or when the serous cavities of the pleura, peritoneum, or large joints are laid open, and a quantity of decomposing material is pent up in an ill-drained cavity. Again, if a large chronic abscess—such as a psoas-abscess—be imperfectly opened and drained, and putrefactive bacteria gain access to it, sapræmia may occur. In these instances the symptoms set in very shortly after the injury—within a few hours.

It has long been held by surgeons, and especially urged by Lord Lister, that absorption of septic products does not take place, or at any rate but imperfectly, after a wound becomes completely covered with healthy granulation-tissue; hence the traumatic fever, the result of septic absorption, comes to an end about the fourth or fifth day. Whether this be correct or not,—and other explanations are more probable at the present time,—it is a fact that sapræmia is a disease of fresh wounds and does not occur after granulation is complete. It may be said here that cases of sapræmia at all comparable to those artificially produced in animals, or to those occurring in obstetric practice, are rare in surgical practice. In a special report on the subject of septic diseases to the Pathological Society of London, 156 clinical records are published, and in 28 of these there were no metastatic abscesses. Of these 28 only two are considered cases of sapræmia, and even these are not above suspicion; it may fairly be urged, however, that these statistics do not give a complete view of the facts, for in a large proportion (24 out of the 26 remaining) this form of toxæmia probably played some part in the production of the symptoms and fatal result; and, secondly, the statistics deal only with fatal cases, and this disease, as is well known, is overcome by proper treatment in a large proportion of cases.

But while acute and pure cases of sapræmia are rare, mild cases are commonly seen; it probably plays a great part in the so-called traumatic fever, that is, in fever occurring immediately after injuries or operations, where sepsis has been allowed to take place in a wound. These mild cases are important from another point of view; the poisons irritate and set up an unhealthy state of the wound, and from their debilitating action on the patient they so lower the resisting powers of his tissues as to make him far more susceptible to the graver forms of septic infection.

Sapræmia, again, is not uncommon in operations on the peritoneum; and there can be no doubt that a good many of the cases of death from exhaustion, and of those cases where there has been fever but no peritonitis, are really cases of sapræmia due to the introduction of non-pathogenetic saprophytic organisms into the peritoneal cavity. Further, the poison being a chemical one, it may readily be absorbed from the

alimentary canal; and it may be remarked that some of the symptoms following strangulation of the gut or intestinal obstruction, usually ascribed to collapse or recurrent shock, are in all probability due to absorption of poisons generated in the intestinal tract above the obstruction.

Symptoms.—The symptoms begin suddenly, and usually appear within twenty-four hours of the time that the discharges from the wound are noticed to be putrid. The temperature rises abruptly to 103°-104° F., or sometimes even higher, being accompanied, but by no means invariably, by a rigor. This initial rigor may be very severe, lasting half an hour or more, and usually is not repeated; in exceptional cases, however, repeated rigors may occur. At the same time the skin becomes hot, dry, and flushed, the patient complains of intense headache, the tongue becomes coated with white fur, and there is intense thirst. Anorexia is complete; vomiting is common, and may be severe even from the commencement. Other common febrile symptoms also appear: the pulse is rapid and full; the respirations are hurried; the urine is scanty, high-coloured, and deposits urates on cooling. Locally a sufficient cause for the above symptoms is usually obvious. The wound may show signs of inflammatory disturbance, or even appear gangrenous; and in all cases there is a considerable amount of very foul-smelling discharge.

If the case be a severe one, and treatment not immediately adopted, signs of severe prostration rapidly supervene. There is delirium, especially at night, at first noisy but soon assuming the low muttering type, and becoming almost constant. There is excessive muscular weakness as evidenced by tremors. The tongue is now dry, brown, and very tremulous; the mouth and lips are covered with sordes. Diarrhœa may come on, and motions and urine be passed unconsciously. The skin may be slightly jaundiced, and petechiæ may appear. The temperature may fall, even to subnormal; coma comes on, and gradually deepens into death. Death usually occurs about the second or third day of the disease; but in other cases may be postponed for as long as a week, the patient passing into a typical "typhoid state," and dying of exhaustion.

In less severe cases, those most commonly seen in surgical practice, the symptoms are similar but less marked. Usually improvement follows at once when the wound is freely opened, the putrid material removed, and free drainage established; but all fever may not cease until granulation is complete. Even in the most severe cases recovery rapidly follows removal of the cause.

A brief abstract of a case quoted by the late Dr. Matthews Duncan, who called special attention to this condition and named it "sapræmia," may be given here, as it serves well to illustrate some of the more marked features of this disease. It is in every respect a pattern case, and indicates the happy result that may be anticipated if treatment be properly carried out.

"A young woman after a natural labour gave birth to her second

child. For the first week slight bleeding took place, and on the seventh day the discharges were noticed to be putrid. The following day, the eighth, rigors occurred, and these were repeated daily until the eleventh day after delivery. The patient was then noticed to be very pale, frequently sick, and there was profuse diarrhœa. The uterus was tender, the breath sweet, respirations 44, pulse 146, temperature 104·2° F. The lochia were copious and stinking. She had been delirious all the previous night. Chloroform was administered, and large pieces of decomposing placenta removed from the uterus, which was thoroughly irrigated. The next day the patient had slept well without delirium, pulse 100, respirations 36, and the highest temperature 101·4°. Recovery henceforth was uninterrupted." Dr. Duncan remarked: "In twenty-four hours the whole aspect of the case changed from despair to hopefulness. The woman was at the point of death, it was apparently not worth disturbing her by treatment, and yet a few hours afterwards she was comfortable, and every alarming symptom had gone." Such recovery as this is only seen in these cases of pure toxæmia.

In the milder cases recovery, when it occurs, is usually rapid and complete; but in the more severe cases convalescence may be accompanied by great anæmia due to the destruction of the red corpuscles and hæmoglobin.

Morbid Anatomy.—The appearances found on post-mortem examination of these cases are very similar to those occurring in animals in whom the disease has been artificially produced. They are somewhat indefinite, and present nothing absolutely characteristic. Rigor mortis comes on early and soon passes off, being in most cases but slightly marked. Decomposition rapidly sets in, and even in cold weather putrefaction of the body prevents proper examination; the organs, eight or ten hours after death, are diffluent or distended with fœtid gases. The blood remains fluid for some time, and gravitates, causing marked hypostatic congestion. Coagulation occurs but slowly, and the clot formed is soft.

The lining membrane of the vessels and endocardium is blood-stained, and there may be extravasations of dark blood beneath the skin, pleuræ, pericardium, in the brain, etc. Occasionally the pleuræ, pericardium, or other serous cavities contain a little blood-stained fluid. The liver and kidneys are usually swollen; occasionally small hæmorrhages are seen in them, and microscopically the glandular cells are swollen and cloudy, or coarsely granular. The spleen is almost invariably much swollen, deeply congested, and occasionally almost diffluent. Various microbes which have been found in the tissues are almost certainly of post-mortem occurrence, and in a few hours they swarm in the body.

Diagnosis presents no difficulty in an ordinary case where we have the sudden onset of febrile symptoms in connexion with an obvious cause. It may not at first be possible to say positively which form of septic disease is present, but the effect of treatment and the progress of the case will decide the question in a few hours. In doubtful cases of

sapræmia and septicæmia the test of treatment must be relied on to exclude the former, the important point being to determine if septicæmia be present.

It must also be remembered that certain symptoms of "collapse" or "shock," on or about the third day after operation, are commonly due to sapræmia. It is probable that a number of deaths after ovariotomy and other operations on the abdomen which have been ascribed to shock and exhaustion are really due to sapræmia.

As to **prognosis** but little need be added. In simple cases of sapræmia the prospect of recovery is always hopeful if treatment be immediately adopted, however bad the patient may appear at the time. In the old and debilitated, however, the prognosis must be regarded as much more serious. Also the risk of other septic troubles arising in connexion with the same cause must be borne in mind, and this cannot be dismissed entirely until granulation is established. Finally, it may be said that recovery, when it occurs, is not only rapid but complete.

Treatment is mainly surgical, and needs but a brief allusion. The two main points to be aimed at have already been indicated, namely, to remove the source of the trouble as thoroughly as possible, and at the same time to injure the tissues as little as possible. The first point is attained by opening up the part freely, removing any decomposing material found, and then flushing all the surfaces of the wound thoroughly with a mild antiseptic lotion. Thus if the cause of the trouble be blood-clot or pieces of placenta or membranes retained and decomposing in the uterus, the cervix must be dilated as far as necessary, the offending substances removed by flushing, or by the fingers, or by curetting as gently as possible, and then the whole uterine cavity thoroughly irrigated. If we have to deal with a wound of one of the large serous cavities, this must be freely laid open, cleansed in a similar way, and means taken to ensure efficient drainage.

The second point is to handle the tissues as gently as possible, and to avoid the use of strong antiseptic solutions for flushing purposes. This flushing only acts mechanically by washing away decomposing material, and does not destroy the organisms present. If strong antiseptic solutions are employed, they act deleteriously on tissues already weakened by contact with the poisonous products of the organisms, and render them less able to resist parasitic invasion. Such fluids as sterilised saline solution or boracic acid are to be preferred. The best temperature at which to use them is probably about 100°-105° F., as this does not damage the tissues, and acts as a general stimulant.

Afterwards the wound must be treated on general surgical principles. At the same time the condition of the patient must be carefully attended to. The cause being removed, rapid recovery will ensue if the effects of the poison already absorbed can be arrested. The collapse of severe cases must be treated by large quantities of stimulants frequently administered. Brandy must be given by mouth, or per rectum if vomiting persist; strychnine seems to be of special value. Carbonate of

ammonia in two or three grain doses may be given hourly, or sal volatile in half-drachm doses. Perhaps the most valuable remedy in these circumstances is the infusion of saline solution in large quantity either into the veins or into the cellular tissue. 10-15 ounces may be injected into the axilla and repeated every few hours if necessary. This dilutes the poison in the blood and hastens its excretion.

In milder cases but little medical treatment is required beyond attending generally to the excretory functions. A diet consisting chiefly of milk with as much fluid as the patient cares to drink may be ordered, a large quantity of fluid serving to dilute the poison and hasten its excretion. If vomiting persist it may be allayed by a simple effervescing mixture, or by small doses of hydrocyanic acid and bismuth, or still better by washing out the stomach. As convalescence is established, a liberal diet with general tonics — iron, quinine, or strychnine—or perhaps change of air will be beneficial.

B. Septicæmia

The pathology of this disease is much more difficult than that of sapræmia. From the description of the experiments on animals given above, it would seem to be very simple, namely, that in sapræmia we have poisoning with the chemical products, in septicæmia we have a blood disease (the organisms growing in the blood or tissues), and in pyæmia we have in addition to blood disease the formation of secondary abscesses; but when we come to the pathology of these diseases as they occur in man, we find that it is not so simple as would appear from the investigations in animals. As a matter of fact, in cases grouped under the name septicæmia, we have not, as a rule, to do with a disease resembling the so-called septicæmia of the lower animals, in which the organisms are growing freely and in large numbers in the blood. True, on examining the blood taken from septicæmic patients, pyogenetic cocci can usually be found; but they are generally in small numbers, are demonstrated with difficulty, and do not, as regards their numbers or distribution, in any way resemble the septicæmia of mice or rabbits: one is thus tempted to consider septicæmia after all as a toxæmia similar to sapræmia, the organisms producing this chemical poison not being in the main located in the circulating blood. In septicæmia, however, we have one marked difference from sapræmia. In the latter case, washing out the decomposing products from the wound, or removal of the part which is the seat of decomposition, at once arrests the disease; the explanation being, as before said, that the organisms producing the poisonous materials are growing outside the body, and that the poisonous materials are absorbed from the surface of the wound; on the other hand, it is evident that in septicæmia the manufactory of the poisonous products is not necessarily in the wound itself, but may be in other parts of the body—in other words, we have to do here with an infective disease

caused by parasitic micro-organisms which are able to live in the body itself.

As to the place where these organisms live and produce their products, I believe, as I have just said, that but a slight effect is produced by the small numbers of organisms found in the circulating blood. The main mass of them are at rest in the system, and from the parts where they are deposited they pour their poisons into the blood.

One of the common seats of these organisms is the tissues of the wound itself which, in an advanced case of septicæmia, may be found infiltrated with the cocci. Although they do not grow freely in the circulating blood, they get into it, and are carried by it and deposited in various parts; after death in cases of septicæmia it is not uncommon to find numerous capillaries throughout the body blocked with collections of cocci which have not yet led to abscesses. In these cases I believe the organisms have become adherent to the endothelium of the blood-vessels, and having succeeded in overcoming the resistance of these cells they grow there, and form the plug which is found after death.

A few cases where the symptoms are similar, though probably more acute, have been found to depend on the growth of organisms in large numbers in the blood—usually bacilli; this condition corresponds to that found in the lower animals. The organisms which are usually associated with septicæmia are, however, the pyogenetic organisms, either the staphylococci, or perhaps more commonly streptococci, but a very similar train of symptoms may result from the presence of other organisms, *e.g.* pneumococci. On post-mortem examination careful search generally shows a few organisms in the blood, and they may be cultivated from the blood of some of the internal organs—more especially of the kidneys, where they are sometimes in considerable numbers. In cases of bacillary septicæmia it seems that the plugs are not uncommon in the heart-muscle. The organisms are always found in considerable numbers in the wound, in the pus, or discharges, in the membranous deposit which is sometimes seen on its surface, and deep in the neighbouring tissues; sometimes in the lymphatics and the neighbouring lymphatic glands.

It is difficult to understand how organisms like these pyogenetic cocci can at one time cause a simple abscess, and at another a severe and rapidly fatal general disease; apparently this depends mainly on the variety and virulence of the organisms. These pyogenetic cocci increase in virulence when injected into the peritoneal cavity, and we find that inoculation from septic peritonitis is one of the commonest causes of the very rapid and fatal form of septicæmia in man. Apart from variation and virulence, the initial dose of the organisms which enters the body has a great deal to do with the result, while predisposition on the part of the body, and the existence of weak points where the organisms can settle and develop are also of great importance. It seems probable that under the term septicæmia several different septic

diseases are grouped; but the possibility of making out the state of the case is becoming more and more difficult, owing to the spread of the principles of antiseptic surgery, and the consequent increasing rarity of the cases—at any rate in the hands of those who would be able to investigate their pathology.

The disease may arise from a simple prick or puncture inflicted during a dissection or post-mortem examination. In these cases the small size of the wound forbids all idea of poisoning by chemical products alone, and the disease which establishes itself is usually extremely rapid in its course, and accompanied by great fatality. Most commonly the disease follows wounds which have not been treated aseptically, and where, consequently, the pyogenetic organisms are present. Why it should arise in one individual with a septic wound and not in another is, as has already been said, not at all clear.

Apart from the virulence of the organisms and the condition of the patient, local conditions no doubt play a very important part, such as much bruising in making the wound, especially of the muscular tissues, in which the organisms can therefore readily settle; the muscles, moreover, are very plentifully provided with lymphatic vessels. Perhaps the most important local cause is the retention of the decomposing fluids in the wound leading to an amount of pressure which helps the entrance of the organisms into the blood- or lymph-stream.

In former times the contagious nature of the disease was well shown by the severe outbreaks which occurred from time to time in the surgical wards of hospitals. The disease once introduced spread from patient to patient with great readiness; most probably being communicated by the surgeons or nurses, especially by the use of the same instruments for dressing successive cases without proper disinfection. More dreaded still was it in some of the large maternity hospitals, where there are records of many outbreaks, especially at the beginning of the last century. In some cases half or two-thirds of the women delivered contracted the disease, and practically all of these died.

The post-mortem changes which are found in septicæmia (apart from the presence of deposits of organisms in various tissues or organs) are almost identical with those found in sapræmia. Rigor mortis is as little marked; putrefaction proceeds with the same extreme rapidity; there are the same blood-changes, blood-staining, serous effusions, etc. The spleen, however, is rarely quite so large, and congestion of the lungs and bronchitis are more or less constantly present.

Symptoms.—In discussing the symptoms, general and local, the severer and more typical form of the disease will first be treated, and subsequently reference made to the milder varieties.

General Symptoms.—The disease commences abruptly, often as early as a few hours after inoculation, usually within twenty-four hours. Accompanying the changes in the wound the temperature is observed to be rapidly rising; rigors occur in more than half the cases, and are usually repeated and severe. The temperature usually remains high

throughout (103°-105° F.), with slight remissions. In the severer cases the patient's life is rapidly endangered; death may occur as early as the second or third day. The pulse is always very rapid, sometimes particularly feeble and irregular; the heart sounds are weak. The respiration is rapid; there may be dyspnœa and cyanosis, accompanied by all the signs of catarrhal bronchitis. There is always complete anorexia, sometimes accompanied by vomiting, more rarely by diarrhœa.

The cerebral symptoms also vary much. There is usually headache more or less severe; in some cases delirium sets in early and is followed by coma,—more usually, perhaps, the mind remains clear to the end. If the case last longer the patient passes into a typhoid state. The skin usually assumes an icteric tint, and purpuric spots may occur. The urine, besides the usual febrile characters, frequently contains albumin, and micrococci (in cases due to them) can usually be detected in it when freshly drawn off from the bladder. The gastro-intestinal symptoms become severe, and the patient dies from exhaustion usually within a week.

Although the differences in the symptoms noted above may possibly depend to some extent on corresponding differences in the causative agent, yet with our present state of knowledge it is impossible to say how far this is the case. No trustworthy observations on this point have yet been made.

The symptoms of the milder varieties of this disorder need only be alluded to: they are those which ordinarily occur in connexion with suppuration and septic wounds. There is always fever, but the temperature rarely reaches 104° F., and rigors are unusual. The patient feels ill, suffers from headache and thirst, the tongue is furred, and there is anorexia. Vomiting may occur, and constipation is the rule. In these cases also micrococci, if carefully searched for, may be found both in the blood and in the urine. As the state of the wound improves the fever subsides and the patient becomes convalescent.

Local Signs.—The changes at the site of inoculation or in the wound also vary greatly. In severe cases from a post-mortem prick the finger in a few hours becomes greatly swollen and intensely painful; thin red lines of inflamed lymphatic vessels may be seen spreading up the arm, and the axillary lymphatic glands become affected. Very shortly the whole arm may become swollen, œdematous, and painful. In rare cases the disease is apparently arrested in the glands, and suppuration occurs there, and also along the course of the lymphatics. In these cases, the abscesses being freely opened, recovery may ensue; but more often the infection rapidly passes beyond them. Sometimes a form of gangrene spreads rapidly from the site of infection. In other cases no suppuration occurs, but the wound becomes covered with a yellowish-white adherent membrane. In this membrane and in the serous flaky discharge bacteria can often be demonstrated. In other cases, again, no marked changes occur at the site of inoculation. In the milder cases the wound is usually in a more or less unhealthy state, suppurating and painful, with swollen reddened margins.

It is probable that some forms of hectic fever may be due to staphylococci growing in the granulations and the tissues bordering on the wound, and pouring their products into the blood-stream. As these organisms are thus growing in the living tissues, according to our definitions as above, some forms of hectic fever must be considered as "chronic septicæmia."

The **diagnosis** may be made with ease and certainty if the case arise in connexion with a small wound (an obvious source of infection), or if the wound present some characteristic state as above described. In other cases extreme difficulty may arise.

The distinction from sapræmia has already been pointed out; from pyæmia it can usually be made by its acuter onset, more rapid progress, more sustained temperature, and, later, by the absence of secondary abscesses. The possibility of a severe or malignant type of specific fever, such as small-pox, may also be borne in mind. The presence of streptococci in the blood and urine may be of help in some doubtful cases. The possibility of overlooking the severer underlying condition, and regarding the case as one of simple severe bronchitis with cardiac failure, must be guarded against. The milder cases with suppurating or septic wounds present no difficulty.

Prognosis in the severer forms is almost hopeless. In extremely rare cases, as has been mentioned, the disease may become arrested and the patient ultimately recover after a prolonged and severe illness, which often leaves him with an impaired constitution. Although persons in apparently robust health may be less liable to fall into the disease, yet when once established it is as fatal in them as in those of weaker constitutions.

Treatment.—On first seeing a case, the wound, if a small one, should be excised, and the parts freely cauterised with pure carbolic acid or the actual cautery. In cases of larger wounds thorough cleansing, followed by application of pure carbolic, may be carried out; or, if they be situated on an extremity, the question of immediate amputation must be considered. These measures, however, rarely arrest the symptoms, the disease running its course unchecked.

As regards general treatment, the chief indication is to support the patient's strength in every way, by administering in small, frequent quantities such nutriment as he can absorb, by giving stimulants—brandy and carbonate of ammonia—freely, and by combating in a suitable way some of the severer symptoms. Thus the temperature may be controlled by tepid sponging, vomiting by bismuth or alkalis, and narcotics may be given where there is pain. The means at our disposal for dealing with the active agent of the disease are more or less imperfect, and consist in the administration of anti-bacterial substances, more especially quinine, in diluting the toxins in the blood and promoting their rapid excretion by the use of saline infusions, and in the employment of the serum of animals immunised against these particular organisms. Quinine should be given in large doses, say 10 grains every

four hours, and continued as long as the patient can stand it. The use of saline solution is of the greatest importance. It is best administered by injection into the subcutaneous tissue, especially of the axilla. From 10 to 15 oz. can usually be injected into the axilla, and this should be repeated every three or four hours in the early stage of the disease. The serum of immunised horses is of doubtful value; usually it is only employed in the case of streptococcus infection, but apparently there are many varieties of streptococci, and the serum derived from one kind is apparently of little use against the others. To meet this point several kinds of polyvalent sera have been tried and are now on the market. The serum, if used, should be given in large doses and frequently repeated.

C. Pyæmia

When we consider the great importance of this disease, and the terrible mortality that it caused among surgical patients up to a recent period, it is very remarkable to find so few references to it in older works, and to note the little interest which it apparently excited among surgeons. Massa in 1559 and Ambrose Paré in 1561 pointed to the occurrence of abscesses in the lungs as the result of head injuries; but no precise hypothesis to account for this was formulated until Boerhaave published his researches in 1720. Boerhaave affirmed that the complications of septic wounds were due to the admixture of the pus of the wound with the blood; and in spite of many adverse hypotheses and criticisms this view received general support and maintained its ground until our own day. John Hunter, while apparently adhering to the view that pyæmia was due to the admixture of pus and blood, demonstrated the existence of suppurative phlebitis, and believed that the walls of the veins secreted the pus. The presence of suppurative phlebitis in almost all cases was also demonstrated by others, of whom we may mention Dance in 1828. In 1834 Gunther, and also Castelnau and Ducrest, injected considerable quantities of pus into the veins of dogs and cats, and succeeded in nearly every instance in producing metastatic abscesses. Virchow, in 1846 and later, pointed out that the material in the inflamed veins is not pus, but softened and altered blood-clot; and that it is cut off from the circulation by more recent blood-clot not yet broken down; and he held that the alleged mixture of blood and pus is really a leucocytosis. He strongly opposed the idea that pus enters the circulation from the veins or from the lymphatic vessels; in the latter case he pointed out that the glands must stop the corpuscles. In 1826 Cruveilhier drew attention to the constant association of suppurative phlebitis with metastatic abscesses. He injected globules of mercury into the circulation of the lower animals, and noticed that abscesses formed where the globules lodged in the vessels; and he believed that pus from the veins lodges and acts in a similar manner. In 1842 D'Arcet stated that purulent infection consists of two phenomena which are quite distinct from each other, but always occur together, namely, poisoning by putrid

products and a blockage of the vessels by emboli; the first leads to fever and general symptoms, and the second to the metastatic abscesses. This view has been more or less accepted by Virchow and others. Virchow further separated septicæmia (which term he also applied to cases of septic poisoning) from pyæmia, and showed that the two might occur separately. Most of the experiments in support of this view were performed with putrid pus: the well-filtered solution, when injected into the veins, produced only septicæmia; the unfiltered solution, containing solid particles, led to pyæmia.

When the importance of bacteriology in connexion with surgery was recognised these views were carried a stage further, and the causal agents were shown to be organisms growing in the decomposing pus. In 1867 Lord Lister first published the results which he had obtained by adopting the germ theory as the explanation of the occurrence of suppuration and septic diseases, and acting thereon; the brilliant success of the antiseptic treatment soon fully confirmed his views, and, in spite of criticism, it has constantly gained greater and greater acceptance, till it is now fully recognised and firmly established. The view now generally held of the pathology of pyæmia is that the general symptoms are due to poisoning with the products of certain pyogenetic bacteria, and the abscesses for the most part to plugging of the blood-vessels with masses of these bacteria, or with emboli infected with them.

Pathology.—Many investigations have been made to determine the organisms which are associated with pyæmia, and it has been found that the organism usually present is the streptococcus pyogenes; though in some few instances, more especially in the less severe forms, pyogenetic staphylococci have been the only ones present. As I have said, the fever and general symptoms of pyæmia may be explained as those of septicæmia; that is to say, they are due to poisonous products poured into the blood-stream by pyogenetic cocci growing in the living tissues of the body. The formation of the secondary abscesses is, however, not altogether quite easy to explain at first sight, for many observers have found pyogenetic cocci circulating in the blood of patients with septic wounds in whom no secondary abscesses were established. Ribbert and others have found that the injection of moderate quantities of staphylococcus pyogenes aureus into the circulation of rabbits is followed, as a rule, only by abscesses in the kidneys, the other organs apparently remaining unaffected; hence other conditions beside the mere presence of pyogenetic organisms circulating in the blood-stream are necessary for the production of the complete picture of pyæmia.

The almost constant presence in these cases of *suppurative phlebitis* has already been mentioned; and there seems no doubt that the secondary abscesses—at any rate in the lungs—are explicable on the view that portions of the softened and infected thrombus become detached and form emboli in these organs. The sequence of events would then be as follows:—(1) Phlebitis occurs in direct connexion with the wound; (2) a thrombus impregnated with micrococci is formed in the vein; (3)

the thrombus softens, disintegrates, and portions of it are carried into the circulation as emboli; (4) these lodge in the first set of capillaries and form infarctions, and then abscesses.

In support of this view are the following experiments:—Ribbert, in experiments on rabbits with staphylococcus pyogenes aureus found that he could produce abscesses in the heart and in various organs if the cocci were injected into the blood-stream attached to particles too gross to pass through the capillaries of these organs. He used a cultivation of the pyogenetic cocci on potatoes, and took care in removing the cultivation to scrape off also the superficial layer of the potato itself. If this mixture of potato granules and organisms was rubbed up with water, so as to form a fine emulsion, and then injected into the circulation, the result was the deposit of organisms in various parts of the body, leading to the formation of abscesses. Bonome found that by mixing cultivations of pyogenetic organisms with finely powdered elder pith, and injecting the mixture into the jugular vein, he obtained similar appearances; but if the fragments of elder pith alone were employed no abscesses resulted.

Various other experiments might be quoted, but these and the pathological facts are sufficient to show that the ordinary pyogenetic cocci are able to cause secondary abscesses in the lungs if they enter the general circulation attached to gross particles, and to establish the importance of thrombosis and embolism as factors in the production of pyæmia. The point of difficulty, however, is to account for the abscesses in organs other than the lungs in cases where the systemic veins are affected; or than the liver in cases where the portal area is the seat of the primary disease. It seems hardly probable that fragments of blood-clot would be able to pass through the pulmonary capillaries and yet stick in the vessels of the kidney and other organs, and some other condition must be found to account for the presence of these further abscesses.

It has already been mentioned, in speaking of the experiments on animals, that Koch found micrococci by means of which he could produce pyæmia; and that the way in which the deposits of organisms were brought about was by their growth in the blood, forming masses of organisms, and more especially entangling blood corpuscles. It is very probable that something similar takes place in man, and that the streptococci growing only in small numbers in the blood tend to form balls, which may be increased by the aggregation of blood corpuscles, and ultimately attain a size which cannot pass through the capillaries. It is possible, also, that in the lungs a fresh suppurative phlebitis may occur in the neighbourhood of the secondary abscesses, and thus lead to the passage of emboli into the arterial circulation. While, however, some of the tertiary abscesses, as we may call them, may be brought about in this way, this view hardly suffices fully to explain the pathology, because it is found that these abscesses are more numerous in certain organs, more especially in the kidneys; whereas if plugs of cocci were floating about in the blood there seems no reason why they should be deposited

more in one organ than in another. There appears, therefore, to be some selective power on the part of the organs, and such an admission clearly invalidates a pure embolic hypothesis. It seems probable that most of these tertiary abscesses occur in this way—that the organisms floating in the blood, in groups not sufficiently large to form emboli, find conditions in certain organs more favourable to their deposit and growth than in others, and establish themselves in the endothelium of the blood-vessels, grow, and form plugs, and subsequently abscesses. Or again, it may be that they find a weak spot, caused by an injury or other factor, in which they can settle; or again, there seems evidence in support of the view I put forward some years ago, which has since received a certain amount of confirmation, that apart from the rupture of blood-vessels and communication with the ducts of secreting organs there may be an actual excretion of the organisms. For example, in the case of the kidney, the organisms may pass from the blood with the water and get into the urinary tubules without any lesion of the wall of the blood-vessel or tubule; and having reached the tubules they may then find conditions, such as rest in a suitable soil, which enable them to develop, and there developing, may form masses and subsequently abscesses. I found distinct evidence of this some years ago in experiments on the lower animals with a certain coccus obtained from wounds, wherein, after injection into the blood-stream, the kidneys were the only organs which showed signs of disease, and the organisms in the kidneys were present in the urinary tubules. This is the most probable explanation of the occasional occurrence of the abscesses in the parotid and other glands sometimes seen in pyæmia.

The suppurations in joints and serous membranes which occur in pyæmia are also probably brought about by the deposit of the organisms in the endothelial cells of the capillaries in these membranes; they grow there, pass into the joint or cavity, and set up the infection.

From what has been said it seems, therefore, that the embolic theory of pyæmia must be extended, and that the occurrence of abscesses in various organs and in the joints must be further explained by supposing either fresh formation of emboli in the circulating blood, or deposit of organisms in the endothelium of the smaller vessels and their growth there; or exit of organisms from the blood-vessels into the tissues in connexion with injuries; or excretion of organisms and their growth in the tubules of the glands, or a combination of these. Various other factors no doubt come into play in the production of pyæmia, such as the dose of organisms, the degrees of their virulence, the general depression of the vitality of the body, and so on; but the above are the essential points.

We must now briefly trace *the changes which take place in the tissues* on the impaction of a septic embolus, or on the development of a mass of organisms in a small vessel or tubule, and result in the formation of an acute abscess. If we make a section through a commencing pyæmic abscess, and stain it appropriately, we shall find that in the centre, obviously in the lumen of a vessel, there is a small deeply-stained

mass which, under a high power of the microscope, is seen to consist of enormous numbers of cocci. Surrounding this is an unstained clear area in which the structure of the tissue is no longer readily discernible; this is an area which has undergone coagulation-necrosis as the result of the action on it of the concentrated toxic products poured out from the central mass of cocci. Outside this zone, where the poison is weaker, the tissues of the part are seen to be undergoing inflammatory changes; at a later period the micrococci burst through the wall of the vessel, and pass into the dead tissue, and even for a certain distance into the inflamed and living tissues; while from the outer part a large amount of fluid plasma and a large number of leucocytes are poured into this same dead area. Among the properties of these organisms is their power of peptonising albumin, and by virtue of this power the necrosed tissues are dissolved, while the effused plasma does not coagulate; thus a central fluid mass is formed, in which are floating large numbers of dead leucocytes and micrococci, and surrounding this mass we have a dense layer of newly-formed granulation-tissue in which the pyogenetic cocci are present.

In man pyæmia may originate in connexion with any inflammation in which the pyogenetic cocci are present; thus it may follow injuries and surgical operations where suppuration is allowed to take place, either from the use of imperfect precautions to ensure asepsis, or from conditions of the case preventing absolute asepsis. In former times this disease was the great dread of surgeons, and the cause of terrible mortality after all operations; but more especially did it follow injuries to veins, bones, or joints. It was most often seen in hospitals, and especially in war, where the hygienic conditions were bad, and many wounded were crowded together. It is interesting to note that so late as the first decade of antiseptic surgery (1869-1878) there were no less than 903 cases of fatal septic disease, chiefly pyæmia, in eight of the large London hospitals.

Acute suppurative osteomyelitis, or periostitis, is a not unfrequent cause of pyæmia, the great tension under which the pus is formed probably forcing the septic emboli from the veins into the circulation. It is not so common after abscesses, boils, and carbuncles; but, in the forms of suppuration, such as spreading cellulitis, due to streptococcus pyogenes, and in acute and chronic middle ear suppurations, pyæmia is not uncommon. It may also follow ulcers of the skin or of the intestinal tract; and in the latter cases the depressed general condition of the patient may promote the occurrence of the disease.

Age.—Statistics point to pyæmia being more common between the years of 30 and 40; but this is probably due to accidental causes: no age is exempt. Its frequency has also been found to vary with the seasons, being more common in damp and cold weather; probably because of the increased neglect of hygienic precautions prevailing at such periods.

Symptoms.—The ordinary form of pyæmia will be first considered, and later the distinctive features of the other varieties. The disease usually commences within the first week of an injury or operation. The wound generally becomes unhealthy, any granulations which have formed

disappear, the previously sealed inter-muscular planes open up, and the discharge becomes thin, watery, or sanious pus, often so scanty that the wound may appear dry. Phlebitis of the veins leading from the affected part may be made out, forming at first tense cords, accompanied later by surrounding thickening and tenderness; and, if superficial, by œdema and redness of the skin. In other cases, as in thrombosis of the lateral sinus, severe pain and tenderness along the course of the vessel may be the main local indication of phlebitis; or again we may have to draw an inference from œdema of the area drained by the vein. In rare cases the wound may appear healthy and even heal, and thrombosis, even if present, may be overlooked.

The *general symptoms* are usually ushered in by a severe rigor and a rapid rise of temperature to 104° or 105° F. For a few days before this there will probably have been some general malaise and loss of appetite, accompanied by more or less fever. The rigor is followed by profuse sweating, and the temperature rapidly falls to 102° or 101° F., or even lower. The rigors are usually repeated throughout the course of the disease; rarely are they absent for more than twenty-four hours at a time, although they occur quite irregularly, and two or more may occur in the course of a few hours, or even in connexion with a single rise of temperature. The temperature is always high during the rigors—104°-105° F.; even 110° F. has been certainly registered; in the intervals of the rigors it may be 100°-101° F., normal, or even subnormal. The rigors are always followed by most profuse and exhausting sweats, and, together with the course of the temperature, are fairly characteristic; they may, however, occur with such daily regularity that the chart resembles that of a case of quotidian ague, or again the temperature may be more continuously high and rigors absent. Profuse sweating is in any case almost constant.

Usually there is anorexia and sometimes vomiting; but occasionally the appetite remains good until near the end, and the digestive functions may be but slightly affected in the earlier stages of the less severe cases. This may be accounted for by the periods of apyrexia or comparative apyrexia, which give the patient time to recover from the effects of the fever. In other cases there may be severe and frequent vomiting, or, more rarely, persistent diarrhœa. The tongue is usually furred, but cleans in the afebrile intervals; later, it becomes brown and dry, and the teeth and lips are covered with sordes. The breath is often said to have a sweet smell. Excessive thirst is common, and the patient will consume a large amount of fluid.

From the beginning the pulse is very rapid and soon becomes soft; later, it becomes very feeble, running, irregular, or uncountable. The first sound of the heart is usually weakened, and may become almost inaudible. Various cardiac murmurs may also be heard; they are usually functional in origin, but in these cases the possibility of infective endocarditis must always be borne in mind. Examination of the blood shows that the white corpuscles are increased in number, relatively and abso-

lutely; and pyogenetic cocci can be seen in the blood, or obtained from it by cultivation. The respirations are increased in frequency; sometimes there is marked dyspnœa and cyanosis, but this usually occurs only in connexion with some bronchial or pulmonary affection, of which, however, it may be almost the only clinical manifestation. The urine usually contains a small amount of albumin, but acute nephritis is very rare. The amount passed is usually about normal, as a large amount of fluid is taken in the diet. The urea and urates are increased, and there is a diminution in the amount of inorganic salts. If blood and pus be present they point rather to a renal abscess. The patient rapidly loses muscular power, the muscles become flabby and waste rapidly, and all movements are very tremulous.

For a long time the patient's mental faculties are retained, or he may perhaps be delirious during the fever, and completely conscious during the intervals. Towards the end of the disease low muttering delirium is common, and the patient usually sinks into a comatose state. In other cases marked cerebral symptoms are present. Wild, noisy delirium and prolonged periods of unconsciousness are seen, and very severe headache is not uncommon. These symptoms are usually the result of the fever: cerebral abscess or meningitis cannot be recognised in the absence of direct localising symptoms.

The skin is often slightly tinged with yellow, but rarely much jaundiced, except in some cases of liver abscess. Occasionally an erythematous rash is seen much resembling scarlet fever in general appearance, but differing from it in its distribution; it chiefly occurs on the parts around the axillæ and groins, and spreading down the limbs, is rarely pronounced on the chest: more rarely still a pustular rash occurs. In the later stages of the disease petechiæ are not uncommon, or extensive cutaneous hæmorrhages may occur. Death usually ensues about the end of the first or during the second week; very few cases live more than three weeks. The patient may die of exhaustion, with all the symptoms of the typhoid state, and coma usually precedes death. Or the patient may die from the direct effects of a secondary lesion, such as cerebral abscess or meningitis, extensive pulmonary disease, heart affection, etc. In rare cases death occurs suddenly from impaction of a large embolus in the pulmonary artery.

The local symptoms, consisting of secondary abscesses in various organs and other parts of the body, and suppuration of the serous membranes, must now be considered. These usually appear about the sixth to the tenth day of the disease; and, in the ordinary form of pyæmia, the emboli originate in the systemic veins, and consequently are most usually arrested in the lungs. The lungs rarely escape secondary deposits in cases of pyæmia arising from disease of bones, such as osteomyelitis or periostitis from compound fractures, amputations, or other wounds involving bones; and in these cases the lungs only may be affected. In other cases, however, abscesses may be found in other parts with or without abscess of the lung; these arise either from the emboli being

sufficiently minute to enable them to pass through the comparatively wide pulmonary capillaries, or from emboli formed in some of the other ways above discussed.

Many abscesses may form in the lungs and yet give rise to no very definite symptoms. The dyspnœa is increased, and there are signs of general bronchitis. If an abscess form near the surface of the lung it will set up a localised pleurisy; then we have the characteristic pleuritic pain, cough, etc., and on auscultation the friction sound. Soon fluid is poured out into the pleura, at first commonly serous, but later becoming purulent; or the lung abscess may burst into the pleura. In either case a localised empyema is formed with or without pneumothorax, and may be recognised by the usual signs. Occasionally an abscess near the surface of the lung is sufficiently large to cause dulness on percussion and the other signs of consolidation.

Pleurisy may also occur apart from pulmonary abscess; and this has been more commonly noted in cases of pyæmia arising in connexion with middle ear disease. The spleen, kidneys, and brain are the other organs most commonly attacked in this form of the disease. In the spleen some pain and enlargement accompanied by great tenderness may be detected, and the abscesses bursting into the general peritoneal cavity may cause acute general peritonitis. Multiple abscesses in the kidneys usually give rise to some pain and tenderness with albuminuria; occasionally all symptoms are absent; or, again, there may be acute nephritis with pus and blood in the urine. The last symptoms are the only trustworthy ones on which to base a definite diagnosis, and they are but rarely seen. Abscesses in the brain and purulent meningitis can only be diagnosed definitely when some definite localising symptom is present; general symptoms, such as headache, vomiting, optic neuritis, coma, and the rest, may occur apart from particular cerebral lesions. Abscesses in the liver also occur, especially it seems after head injuries. They arise in connexion with the branches of the hepatic artery, and thus differ from those of portal pyæmia.

The eyes may also be affected in a very important manner: optic neuritis may occur with hæmorrhages scattered in the retina; the arteria centralis retinæ may be plugged by an embolus; this causes sudden blindness of the affected eye, followed by suppuration of the eyeball—panophthalmitis. The latter result will also follow if an embolus lodge in the ciliary region or iris.

Suppuration in the joints is one of the commonest lesions of pyæmia, and may occur in any joint. There is usually intense pain at the onset, rapidly followed by purulent effusion, and then the pain often subsides more or less completely. The joint shows all the signs of acute suppurative arthritis, but if the affection be treated early by free evacuation of the pus, it is remarkable how little permanent damage may follow.

Suppuration in the peritoneal cavity also not uncommonly occurs; and may be primary, or secondary to an abscess of one of the viscera which may burst into it. It is very common in puerperal cases, in some

probably due to direct extension. It is usually general, but may be localised at the outset. Pain at first is severe, and accompanied by all the symptoms of acute peritonitis; later, however, pain and tenderness are often both absent; excessive tympanites from paralysis of the intestines is present; and, the purulent effusion being distributed throughout the abdomen, but nowhere in large quantity, dulness or fluctuation may never be obtainable. In this absence of signs the affection is commonly overlooked.

Purulent effusion in the pericardium may also occur, sometimes preceded by signs of pericarditis, friction sounds, etc., but often coming on very insidiously.

In the cellular tissue of the body large abscesses may form and burrow extensively. There is usually severe pain at the outset, but afterwards this may subside; the swelling is often very diffuse, and tenderness may not be very marked. Transient patches of œdema and redness of the skin and subcutaneous tissues, subsiding without suppuration, are also described (Erichsen). Abscesses in the muscles are very rare. In the heart they are also rare. The symptoms are indefinite, but the cardiac action is greatly impaired, and death is liable to occur from rupture of the heart wall. In rare cases abscesses are seen in the parotid gland, thyroid gland, and testicles. Their possible pathology has been discussed.

Morbid Anatomy.—After what has already been said, this may be dealt with very briefly. The general blood- and tissue-changes are exactly similar to those already described in septicæmia, but are usually somewhat less marked. They are the effect of the fever and general blood poisoning.

The wound will be found as already described, and if careful search be made, a thrombosed vein will often be found leading from it. Such veins are filled with soft adherent clot, in some places breaking down, in others replaced by pus, which is always shut off by clot from the general circulation. Around the vein there is a certain amount of periphlebitis, or even a periphlebitic abscess. Cases have also been seen (six cases, *Path. Soc. Reports*) in which thrombosis followed by embolism has occurred in a vein remote from the seat of infection.

In the lungs signs of bronchitis and broncho-pneumonia are almost constantly found. Hæmorrhagic infarctions are rarely seen, but scattered throughout the organ are abscesses varying in size from a pea upwards. In the kidneys and spleen also the abscesses are commonly multiple. In the brain it is not uncommon to find a large area of acute softening, the result of an embolus, with only a drop or so of pus in its centre. Pyogenetic organisms of one or more varieties can be demonstrated in large numbers in the original site of infection, in the emboli and thrombosed veins, and in the secondary abscesses; but rarely in the blood.

Suppurative Pylephlebitis or Portal Pyæmia will be discussed elsewhere (see vol. iv.).

So-called **Chronic Pyæmia** *or* **Multiple Abscesses.**—This disease, arising under similar conditions to true pyæmia, and leading to the formation of secondary abscesses, has long been confounded with pyæmia. It differs,

however, essentially from true pyæmia in that embolism apparently plays no part in it. Pyogenetic organisms reach the blood-stream by a wound, or the like, and, owing to the depressed vitality of the patient, continue to live there but produce only slight disturbance. Then if some spot be weakened as the result of a slight injury, the organisms fix on that spot, develop in it, and produce an abscess. The injury producing the abscess is usually slight, such as a strain, too long or too great pressure on a part, and so forth. The abscesses are consequently few in number, often only one or two, and are situated in the subcutaneous tissues or in the joints. The disease may last for months, the general symptoms not being severe; elevation of temperature, pain, etc., occur at the commencement of each fresh abscess, but subside in the intervals.

A case is recorded in the Pathological Society's *Transactions*, in which a compound fracture of the lower jaw was followed by suppuration occurring at the site of other fractures sustained at the same time. The fracture of the femur was noticed suppurating nearly a month after the injury, and ten days later the fractures of the humerus and rib were affected. Numerous experiments on animals have shown that the simple injection of small numbers of pyogenetic cocci into the blood-stream will be followed by no ill effects, but that if simultaneously an injury be inflicted on any part of the body a local abscess may result.

Diagnosis of Pyæmia.—Difficulties mainly arise in cases where the source of infection is unusual or obscure; it must also be borne in mind that a patient with a suppurating wound may contract a fever, such as typhoid. In all suspected cases such sources of infection as osteomyelitis, chronic middle ear suppuration, infective endocarditis, suppuration in the nose or in connexion with carious teeth, ulceration of the mouth, throat, or alimentary tract, rectal diseases, gonorrhœa, and so forth, must be very carefully inquired into.

Of the diseases more or less resembling pyæmia, typhoid fever is the most important; indeed, pyæmia has been called wound-typhoid. In both we find a similar temperature, and in both an enlarged spleen; similar abdominal symptoms may also be present; in both the typhoid state supervenes, and there may be an absence of other definite symptoms. To distinguish typhoid we must inquire into a possible source of infection; the rose rash and peculiar stools are decisive; hæmorrhage from the bowel is extremely suggestive; the abdominal symptoms may be prominent, and the fever is usually more regular; and if the disease has gone on for more than a week the agglutination reaction should be present. Moreover, in very rare cases pyæmic infection may arise in connexion with the typhoid ulcers. On the other hand, pyæmia is indicated by the discovery of a probable source of infection, by the irregular course of the temperature, by the recurrent rigors and profuse sweating, by petechiæ in the skin, by optic neuritis and retinal hæmorrhages, and, lastly and conclusively, by the formation of multiple abscesses.

Typhus fever, now extremely rare, also closely simulates pyæmia. The abrupt onset, high fever, and cerebral symptoms are common to

both. The diagnosis between them must rest on the mulberry rash of typhus, or on the secondary abscesses in pyæmia. In acute tuberculosis the temperature may be similar, and there may be no decisive symptoms. We must look for other signs of a tuberculous disease and a tuberculous history. Later, the slower onset of the disease, its protracted course, tubercles in the choroid, and the absence of local signs of abscess, show the true nature of the disease.

Pyæmia may closely simulate malaria in the course of the fever and sweatings. The history of exposure to malarial influences, or previous attacks of it, the absence of local abscesses, the detection of the malarial parasite, and subsequently the effect of quinine, will decide the question. Acute rheumatism and pyæmia have in common a similar course of temperature, profuse sweats, inflammation of serous membranes and joints, and perhaps endocarditis. In acute rheumatism the sweat has a very peculiar sour odour; the inflammation of the joints often subsides suddenly and attacks other joints, and there is no jaundice or sign of embolism. With regard to infective endocarditis, it must be remembered that the murmur varies much, and may be absent.

The differences between the rash of scarlet fever and a skin affection sometimes seen in pyæmia have already been pointed out, and these diseases have few other symptoms in common.

The diagnosis from septicæmia is not important, and rests entirely on the presence of secondary abscesses.

Pyæmia may have to be distinguished from meningitis when head symptoms are very prominent, or from uræmia in cases of acute nephritis. Glanders in the human subject may also closely simulate pyæmia, but the examination of the pus from the abscesses will often lead to the discovery of the glanders bacillus.

In the **prognosis** of pyæmia the varieties of the disease must be separately noticed. Cases of infective endocarditis and suppurative pylephlebitis are invariably fatal.

In ordinary surgical pyæmia the prognosis is very grave and recovery extremely rare. The majority of the patients die in the first week, and very few survive more than two weeks. The worst cases are those associated with high continuous fever, extreme vital depression, and the early formation of visceral abscesses. In the cases which recover, as a rule only external abscesses have occurred; and even then an impaired constitution, stiff joints and tendons usually remain. In cases of chronic pyæmia, on the other hand, recovery is not infrequent, but after months of suffering and with the deformities above mentioned.

Treatment.—The preventive treatment may first be considered. This is purely surgical, and consists in the thorough adoption of antiseptic methods wherever possible. In other cases every precaution, and especially free drainage, must be adopted to keep the wound as healthy as possible. At the same time the patient's general health must be carefully attended to, a good supply of fresh air provided, and overcrowding, especially of patients suffering from suppurating wounds, must

be avoided. Even where thrombosis of a vein has occurred in connexion with suppuration the pyæmia may be cut short by freely opening up, purifying, and draining the source of infection, and at the same time cutting off from the circulation and cleansing, or, much better, excising the whole of the thrombosed vein.

The disease once established, nothing but symptomatic treatment can be attempted. The fever, if very high or continuous, may be controlled by antipyretics, or better still by such means as tepid sponging. Quinine in 10-grain doses every four hours should be given: antistreptococcic serum may be employed. Cardiac failure must be mainly combated by stimulants, of which brandy or whisky are the best, and these may be given in large quantities. If vomiting be present, champagne may be tried. Severe vomiting may be allayed with bismuth or small doses of hydrocyanic acid. Morphine is required in many cases to relieve pain. The patient's general health must be supported by abundance of such light nourishment as he can digest; and an unlimited quantity of fluid, such as barley water, "imperial drink," milk, and soda-water may be allowed. Special care must be taken in the nursing to avoid bed-sores. Secondary abscesses must be promptly opened and drained.

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For References, see p. 904.

ERYSIPELAS

By W. WATSON CHEYNE, C.B., F.R.S.

Definition.—A contagious disease characterised by a well-defined spreading inflammation of the skin, or more rarely of a mucous membrane, due to a specific micro-organism, and associated with general febrile symptoms.

The contagious nature of the disease was not recognised until about 1850, and apparently first in England. Later Velpeau pointed this out in France, and showed, as Trousseau had previously done, the frequency of the disease in connexion with a wound or abrasion. In Germany Wernher in 1862, and Volkmann in 1869, adopted these views. This contagious nature has now been conclusively proved, and that the disease originates almost invariably in connexion with slight wounds or abrasions is generally admitted; but there is even yet much dispute as to the exact limits of the name. The older authors applied it to a large number of distinct skin affections (such as eczema, etc.), and also to diffuse phlegmonous inflammations of internal organs and serous membranes. The skin affection known as erysipelas is now sharply

distinguished, and the name is not applied to internal inflammations; though some authors, following Nunneley (1841), still describe as erysipelas spreading diffuse forms of inflammation affecting the subcutaneous tissues with or without associated skin affection, and even such diseases as whitlow.

It seems more in accordance with the present state of our knowledge to regard inflammation of the subcutaneous cellular tissue as a distinct (although a closely allied) affection due to a separate cause; and when the two affections occur simultaneously and run concurrently, to look on them as due to a mixed infection. This subject must be further considered when the specificity of the causative micro-organism is discussed. A distinction has also been drawn between surgical erysipelas, or that complicating wounds, and medical erysipelas, which latter mainly attacks the face and is supposed to arise idiopathically. Usually, however, it arises in connexion with some slight injury of surface, and there is no essential difference in the two diseases. Although typically a skin affection and limited to the cutis vera, the disease may attack mucous membranes, either spreading to them by direct extension from the skin, or, originating on them: the commonest situation is the pharynx, where the disease may follow or precede an erysipelas of the face.

Etiology.—The causes of this affection may be either general or local, some perhaps act both generally and locally. The disease is widely spread, and usually occurs in an endemic form; rarely distinct epidemics have been noted. Women are more liable to it than men, and people between the ages of 35 and 55 are chiefly attacked. *Season* seems to exert a decided influence on its prevalence, the disease being most common in spring and autumn, much less so in summer and winter. February and November are the months in which it is more especially prevalent,—months, that is, usually associated with considerable changes of temperature, but on the whole cold and damp. This may be in part accounted for by the overcrowding in unhealthy, ill-ventilated rooms, and the want of proper exercise, which commonly occur at such seasons.

Erysipelas formerly was not uncommon in the surgical wards of hospitals, and especially in those which were ill ventilated or defective in sanitary arrangements. In these wards, if once introduced, it was extremely difficult to eradicate, and nearly every patient with a wound would be attacked, the *contagion* being probably conveyed by the hands of the dressers, etc. Where the hygienic arrangements are good, and efficient means are taken to prevent direct conveyance of the contagion by the hands or instruments, the disease shows but little tendency to spread; the poison is never widely diffused through the air. It clings closely, however, to furniture, bedding, clothes, and the like, and may be conveyed by a third person. Erysipelas is not uncommon in patients debilitated by recent acute diseases such as typhoid fever; and in general it is more common among the poor and weakly, whether from improper food, bad hygiene, or the exhausting effects of chronic disease, especially perhaps of albuminuria and diabetes.

Certain persons show a marked disposition to the disease, and suffer from many attacks of it throughout their lives: the attacks sometimes show a kind of regularity, returning every spring or sometimes even more often, and this disposition has been said to be hereditary. It may be in part a general disposition, but many cases may possibly be explained by the constant presence of a chronic disease producing a weak spot or slight abrasion from which the disease originates; in favour of this view it is found that the same spot is attacked time after time. Thus such persons may be found to suffer from an irritating discharge from the nose or ears which excoriates the surrounding skin. It is probable that one attack confers *immunity* for a very short time; it has been found impossible to inoculate successfully a patient who had had an attack five weeks previously; a second attack, however, may occur after three or four months.

The most important disposing condition is *a wound*, which may be of any size; the smallest abrasion, by removing the epidermis, seems sufficient to allow the organisms to gain a foothold. This advantage may be given not only by trauma, but by irritating discharges from ozæna, otorrhœa, or even a common cold; or by chronic eczema, lupus, and the like. It has frequently been asserted that a small wound, such as one of these, is invariably the starting-point of the disease, and that, as Volkmann says, erysipelas is a true traumatic infective disease. This view is most probably correct, for if very careful search be made, some wound or abrasion will be found in the great majority of cases; for the others it must be remembered that the wound may have healed during the incubation period of the disease, and that if the disease be not seen at its commencement, the swelling, etc., that occurs will soon mask it. The fact that the disease on the face generally starts at the margins of skin and mucous membranes, or near the external auditory meatus, where excoriations are so common and so easily overlooked, lends much support to this view. In searching for wounds it may be remembered also, as Fehleisen has shown, that the redness may first appear at some little distance (3 cm.) from the point of inoculation.

The immediate cause has been most conclusively shown by Fehleisen to be a streptococcus very closely allied to, if not identical with, the *streptococcus pyogenes*. Micrococci of various kinds had been previously recognised in the blood and lymphatic vessels of the skin of the affected part, chiefly at and just beyond the spreading margin of the disease, by such observers as Lukomsky, von Recklinghausen, Koch, and Billroth. They also described the cocci as occurring in the subcutaneous tissues and in the internal organs; indeed, there is a great probability that most of their observations were made on cases of erysipelas complicated with cellulitis or pyæmia. Fehleisen was the first to describe accurately and to isolate a specific streptococcus, to obtain it in pure cultivations outside the body, and to demonstrate its direct causal relationship with the disease. On examining *sections of skin* taken through the margin of the spreading redness, he observed numerous micrococci growing in

chains in the lymphatic vessels and spaces of the corium, not in the blood-vessels as other observers had stated; these he found to be most numerous at and just beyond the spreading margin of the disease, but in parts where the redness is passing or has passed off, the lymphatic vessels and spaces become infiltrated with leucocytes and the cocci rapidly die out. A few cocci may also be seen in the neighbouring subcutaneous tissues. Pure cultivations are readily obtained on various nutrient media,—blood-serum, nutrient gelatine, potatoes, etc. Fehleisen asserts that their growth in these media is characteristic, but most observers have failed to detect any difference between it and that of streptococcus pyogenes.

Experiments were made by *inoculating* the ears of *rabbits* with pure cultivations. A definite disease followed, characterised, as in man, by a sharp spreading margin of redness without suppuration. On making sections of the spreading margin the cocci were found in the lymphatic vessels and spaces presenting the same appearances as in man. Other organisms may, however, produce similar results in rabbits. Further, by *inoculating persons* the subjects of incurable tumours with pure cultivations of the cocci, Fehleisen has absolutely proved that these organisms are the cause of erysipelas in man. Of seven individuals so inoculated, six presented the disease in every way typical; the seventh case failed even after repeated inoculation, but he had suffered two or three months previously from an attack of erysipelas, and was probably immune. It was shown in some of the other six cases that immunity was conferred for at least a short time, as repeated subsequent inoculations failed to reproduce the disease. The method he employed was to make superficial scarifications over the part, and then to rub in the pure culture. The incubation period in these cases varied from fifteen to sixty-one hours, and it was also noted that the disease did not always start exactly at the punctures, a fact which has also been noted in cases occurring spontaneously.

It had long been noted that various malignant diseases—especially sarcoma [*vide* p. 637, "Treatment of New Growths"] and such chronic skin diseases as lupus and chronic eczema—may be markedly improved or even cured by an attack of erysipelas; and many observers had endeavoured with more or less success to set up in such cases a *curative erysipelas.* It was for this reason that Fehleisen's experiments, which at first sight might appear unjustifiable, were undertaken; considerable benefit occurred in most of the cases, although probably none were cured. This treatment, almost abandoned because of its danger, has lately been revived in an improved form for the cure of some forms of malignant disease, the toxins of erysipelas obtained by sterilising a pure cultivation of the cocci being employed as a hypodermic injection.

An important question has been raised by a number of observers, who have asserted, and many still assert, that the *streptococcus of erysipelas* is identical with the *streptococcus pyogenes*, and that the different results of their action depend on differences in other conditions, such as variation in

the virulence, dose, seat of inoculation, susceptibility of the host, and so forth. Fehleisen asserted that in cultivations under similar conditions there were marked differences in the modes of growth of the two forms, and also that the inoculations in rabbits gave rise to similar but distinctive processes. Other observers, however, have totally failed to confirm these results. There is no doubt that the two organisms are very closely allied species, but that they are absolutely identical seems difficult to reconcile with clinical experience in man. On the one hand, there is no sufficient evidence to show that the erysipelas cocci can cause suppuration in man —this result has never followed experimental inoculation with pure cultivations—and, on the other hand, inoculation into the skin of *streptococcus pyogenes* has produced suppuration, but not erysipelas. Thus, in opening abscesses which contain streptococci, the skin is necessarily inoculated; and in one definite case (Rosenbach) a dense inflammatory induration appeared round the incision, but erysipelas has never been shown to result in such cases. The balance of evidence, therefore, seems to be in favour of the specific nature of the erysipelas coccus, but the point is still under discussion.

Some further experiments illustrating the mode in which the disease is spread may be alluded to. It has been found extremely difficult to transmit the disease directly from patient to patient, and prepared plates exposed to the air of wards containing cases of erysipelas have very rarely yielded cultures of the organism. They have been most successful when the patients were freely *desquamating*, the scales thrown off having been shown by cultivation to contain living organisms. Thus it is probable that these scales are the most usual means of carrying the disease.

Morbid Anatomy.—The minute anatomy of the local lesion has already been described, and as it will be further discussed under the symptomatology, but little need be said in this place. The redness of the skin disappears after death, but some of the swelling remains; blebs and effusion into the lax subcutaneous tissue are also seen. These blebs usually contain serum more or less turbid; they rarely contain organisms. The loose tissue of the eyelids, larynx, etc., is also distended with serum, and the tension of the effusion may be so great as to cause gangrene of these parts.

In patients dying of erysipelas the characteristic appearances of the more fatal complications will also usually be found. Thus in many cases diffuse *cellulitis* will be seen, and often a resulting *pyæmia*. Disease of the kidneys must also be looked for. In such cases organisms are commonly found in the internal organs, but this is probably not so in simple cases of erysipelas. *Pneumonia* or *bronchitis* may also be found, more rarely *meningitis*; the latter has been said to arise from the inflammation passing directly inwards from the scalp to the meninges, or from the face along the trunks of the fifth nerve, but it is more probably a pyæmic symptom. If a person die of simple uncomplicated erysipelas, the internal organs simply show the usual signs of a septic disease or

those common to the *typhoid state*, namely, swollen congested spleen, enlarged liver, and kidneys with cloudy degeneration of the glandular epithelium, etc.

Symptoms.—Several varieties are described. In addition to the ordinary form, cases occur of so-called "wandering" erysipelas, where a patch of redness appears at one part, spreads a little, and then after three or four days dies away to reappear elsewhere, constitutional symptoms usually showing themselves with the appearance of each fresh patch. The most serious form is that described as "phlegmonous" or "gangrenous" erysipelas; but, as will be mentioned presently, it is probable that these are cases of mixed infection. The incubation period of erysipelas has been variously estimated at from three to seven days. We have already seen that it is fifteen to sixty-one hours when the disease is experimentally produced. The general symptoms commence somewhat abruptly, simultaneously with, or just before or after the appearance of the local lesion. The temperature rises rapidly; there is often a more or less severe rigor, the patient feels ill, is languid, and often has intense headache, anorexia, or even vomiting. The fever and constitutional disturbance are usually in direct proportion to the extent of the local lesion. Herpes labialis is not uncommonly seen, and, apart from cases of erysipelas of the fauces, there is soreness of the throat accompanied by general congestion. The fever, with varying remissions, usually remains high while the skin affection is spreading, and often terminates suddenly with the cessation of the spread. The skin is hot and dry, but sweating occurs during the remissions of the temperature. Other febrile signs, such as rapid pulse, frequent respirations, febrile condition of urine, are also present, usually in direct proportion to the degree of the fever. In some cases after apparent cessation of the symptoms a *recrudescence of the disease* takes place, a fresh rise of temperature, etc., accompanying a fresh local outbreak. In the chronic cases of *wandering erysipelas* the temperature takes a very irregular course; it may become normal while the disease is still spreading, but usually a fresh spread is accompanied by marked but brief constitutional disturbances.

In the milder uncomplicated cases the general disturbance may be and usually is very slight; in other cases, more especially in debilitated constitutions, the gravest symptoms may supervene. The severity of the fever and its duration may bring on the typhoid state, and the patient sink of exhaustion. In other cases severe *gastro-intestinal disturbances* may be present—complete anorexia, obstinate vomiting accompanied by constipation or profuse diarrhœa—and these symptoms persist and exhaust the patient. Of albuminuria I shall speak later. In other cases, again, and especially in drunkards, *nervous symptoms*, such as intense headache and great restlessness accompanied by violent delirium, may be very prominent from the commencement. The delirium may pass into the low muttering type as the patient sinks into stupor, coma, and death. In most of the severer cases the *spleen* may be somewhat enlarged, and the skin is more or less jaundiced.

Locally, the disease as it attacks the face and head will be alone described. A sharply defined patch of redness appears on the cheeks—or more usually at the junction of the mucous membrane of the nose and skin—at the margins of the lips, near the external auditory meatus, or near the margin of the hairy scalp. The affected portion of skin becomes red, hot, swollen, and shiny, and is accompanied by a feeling of tension or burning pain; the patch spreads by direct continuity to surrounding parts. Extension usually occurs unequally in different directions, and the disease is very apt to be arrested by a fold in the skin or at the margin of the scalp. Where it is spreading there is always a sharply defined, raised red line, separating the healthy from the affected tissues, which may be both seen and felt. Behind this line the redness and swelling gradually shade off until the parts become normal again. The disease lasts in a particular spot for about four or five days, so that it may still be spreading in another place while the part first attacked has become normal. Where the disease spreads over loose tissues much serous effusion oozes into them; thus the eyelids become enormously swollen, and the eyes are closed, the ears are greatly thickened, the wrinkles of the face obliterated, and the features quite unrecognisable. Blebs more or less large may also appear on the skin in the severer cases and add to the deformity. They contain serum, often turbid, or a sticky gelatinous fluid, and soon burst and dry up, leaving adherent crusts. Very rarely local gangrene may occur from the intense virulence of the inflammation and the tension of the effusion in such tissues as the eyelids, ears, etc. In such cases the eye may be destroyed. The neighbouring lymphatic glands are always enlarged and tender.

Definite *abscesses* occurring in the skin or subcutaneous cellular tissue are most probably the result of a mixed infection, and this is not unlikely to be the case when they occur, as is not very uncommon, in the eyelids.

When the disease spreads to *the scalp* there is usually increased headache accompanied by much local tenderness and œdema, but without marked redness. The disease may spread from the face to the neck and body. In some cases it assumes a chronic form, spreading from place to place until nearly the whole body has been attacked, and one part may even be affected twice. These cases are more common in children; the constitutional disturbance varies, but, as a rule, is mild, and recovery may take place after many weeks; in infants, however, recovery may be incomplete, and death occur later from marasmus. In these cases also the spreading margin of the disease is no longer distinct, but diffuse patches appear, often not in continuity.

Where the disease spreads over a joint, effusion takes place into its cavity. This is serous, perhaps turbid, but probably in simple erysipelas never purulent. Wherever the skin has been attacked considerable desquamation follows, and this, as has already been shown, is the chief means of dissemination of the disease.

I have already said that the various *mucous membranes* may also be

attacked by erysipelas; the frequency with which this occurs varies in different epidemics. The disease may begin on the skin and spread by direct continuity to the mucous membranes of the nose, mouth, etc., or conversely; or, beginning at the junction of skin and mucous membrane, may extend simultaneously in both directions. There is also good reason to believe that some of the cases described as acute œdematous laryngitis and pharyngitis are really examples of erysipelas limited to that region. The disease always spreads from the throat to the skin, or *vice versâ*, by direct continuity; and cases have been described which illustrate the four paths by which this extension may take place. In order of frequency they may be enumerated as follows: (1) from the lips by the mucous membrane of the mouth, tongue, etc.; (2) through the nostrils, nasal mucous membrane, etc.; (3) by the Eustachian tube and auditory canal; (4) from the eyes by the lacrimal canal to the nose, etc. The mouth, ear, nose, tongue, palate, pharynx, larynx, and trachea may all be affected. Cornil records eighteen cases in which the throat was attacked; in nine of these the affection spread inwards from the skin, in seven it originated in the throat. In the former case the throat was generally attacked on the third to the fifth day of the disease. In all these cases the general symptoms are much more severe, and gastro-intestinal disturbances are common. The throat is extremely painful, preventing sleep, and causing great pain and difficulty in swallowing. When the larynx is attacked there is the further danger of suffocation from laryngeal stenosis; or the disease may spread down the trachea, and broncho-pneumonia may be set up.

The local appearances on the palate and fauces are most characteristic. The whole part is uniformly dark, shiny, red, and feels dry and burning hot. Much œdematous swelling also occurs, especially affecting the uvula; the tonsils share in the process, but are not nearly so enlarged as in quinsies, and sometimes the sharp spreading margin of the disease may be distinctly seen. Bullæ, small or large, are frequently present; at first they are well formed and contain turbid serum, but in a few hours they burst, leaving yellowish-white, membranous-looking patches, which persist some days. After the disease has subsided, dilated veins are observed on the part.

When the nose is attacked the swelling of the mucous membrane entirely occludes it. In the mouth erysipelas gives rise to marked purplish-red swelling and profuse ptyalism. In all these cases the glands at the angles of the jaw are markedly swollen and tender, causing great pain and difficulty in mastication.

When the larynx is attacked there is deep red congestion and swelling of the whole mucous membrane, and great œdema, especially affecting the epiglottis, aryepiglottic folds, and arytenoids. This œdema always comes on very suddenly, and may rapidly destroy the patient's life unless urgent means of treatment be adopted. In rare cases the inflammation goes on to gangrene: this usually attacks the œdematous parts, or arises in the membranous patches above described. All the symptoms are then

aggravated, there is intense prostration, the breath is extremely fœtid, and septic forms of bronchitis and pneumonia may set in.

Two other forms of the disease may be briefly mentioned. In infants the disease may start in connexion with *the navel*, and, though commonly fatal from the feeble resisting power of the patient, it presents no other peculiarity. Also in infants or young children the disease is not uncommonly seen to start from the *vulva*. Intense swelling and œdema of these parts occur, with pain and great difficulty in micturition; not very uncommonly it results in gangrene.

Complications and Sequels.—The most serious local complication of erysipelas is diffuse cellulitis; this it is which gives rise to local suppuration, to pleurisy, pericarditis, meningitis, and the other pyæmic symptoms usually described as complications of erysipelas. Apart from septic infection, pneumonia and bronchitis are occasionally seen, especially if the throat be affected.

Albuminuria is very commonly present as a symptom of erysipelas, and acute nephritis is not very rare. In drunkards delirium tremens may arise. In rare instances, by implication of the conjunctiva, the nutrition of the cornea may suffer, leading to sloughing and destruction of the eye; if the disease spread along the ear and Eustachian tube acute suppuration of the middle ear, with all its evils, necessarily ensues.

Among sequels may be noted increased liability to the disease after a brief period of immunity; and repeated attacks not uncommonly leave a greatly thickened, unsightly condition of the skin. When the scalp is attacked there is usually a falling off of the hair, which, however, soon grows again, unless the attacks be repeated. Chronic skin diseases—eczema, lupus, etc.—are often much reduced, or even cured, by an attack of erysipelas; in many cases after single attacks it has been noticed that the skin is finer and softer, and the complexion much improved.

The **diagnosis** of erysipelas of the skin is usually quite easy; the abrupt raised margin of redness, spreading by direct extension, and accompanied by constitutional disturbance, is characteristic.

Diffuse cellulitis is accompanied by more brawny swelling, and the superjacent redness of the skin is more diffuse. The redness accompanying lymphangitis is also more diffused, and, at least in parts, the thin red lines of the larger inflamed vessels may be made out.

Erythema of the skin occurs in bright red diffuse patches, and spreads by the formation of fresh distinct patches. It chiefly resembles the migratory form of erysipelas, but is not accompanied by pain or any constitutional disturbance.

Acute eczema spreads by the formation of tiny, pin-point lesions, usually minute vesicles; it has a weeping surface, and never anywhere a distinct raised margin. Other skin affections—such as herpes, pemphigus, and urticaria—need scarcely be mentioned.

In the throat, also, erysipelas presents characteristic points apart from its general association with skin affection. The pharynx is more acutely painful, the constitutional disturbance greater, the local signs of swelling

and œdema more marked, and the parts of a deeper red than in simple acute pharyngitis. The tonsils are not nearly so large or inflamed as in quinsy. Herpes of the palate is not associated with so much general congestion or swelling, and the constitutional disturbance is slight. The severe bodily prostration accompanying erysipelas of the larynx is the chief sign in distinguishing it from other forms of acute œdema. Scarlet fever may simulate both the throat and skin affection; but the scarlet rash never appears first on the face, and is more diffuse and punctiform both on the skin and throat. The pultaceous throat sometimes met with in scarlet fever may, however, be indistinguishable from that following the formation of vesicles in erysipelas; the diagnosis must then be made by the concomitant symptoms.

The **prognosis** of erysipelas, as it occurs in healthy adults, is very favourable; but some epidemics are much more severe than others. Mild cases last two or three days; the severer ones five to ten days; the migrating form may last for weeks, and in any case after apparent cessation relapses may occur.

Erysipelas attacking surgical or puerperal patients is apparently much more fatal than the kind above described; but the mortality formerly occurring in such cases was probably due in part to the lowering treatment (bleeding and so forth) too often adopted in patients already depressed; and in part to other complications of the wound. The disease is more fatal in the aged; and in infants it tends to assume the spreading form which not unfrequently leads to marasmus and death.

In patients suffering from chronic renal disease the prognosis is extremely bad; it is also grave in the subjects of chronic alcoholism or of any wasting disease such as diabetes, pulmonary tuberculosis, malignant disease, chronic suppuration, and the like.

Cases in which the throat is attacked are more dangerous than those in which the skin is affected alone; and those cases in which the disease spreads from the skin are said to be much more dangerous than those in which the extension takes place in the opposite direction. When the larynx is involved the case becomes extremely grave, apart from the special danger of suffocation. Gangrene of the throat is almost necessarily fatal.

In most cases the severity of the general disturbance, the pulse, temperature, gastric and mental symptoms will give trustworthy data on which to base a prognosis.

Treatment.—The disease being contagious, the patient must be isolated as soon as possible; especially must he be kept away from all communication with patients suffering from wounds, and from puerperal cases. The attendants on the sick must also be very careful of any cuts, cracks, or abrasions on their hands, and they must not at the same time look after other patients, especially those suffering from wounds. If these precautions be rigidly carried out, and other cases treated aseptically, there is little harm in the patient remaining in the same ward with

them. On recovery the patient's bed, clothes, and other articles must be thoroughly disinfected, and the walls and furniture around well washed. During convalescence, when desquamation is in progress, increased care must be taken; the patient's skin should be well greased with vaseline or olive oil, or, if the area be small, with carbolic oil (1-40), and sponged with a weak solution of permanganate of potash many times a day until the process has come to an end.

In the ordinary milder cases seen in adults no active medicinal treatment is required. A light, nutritious diet, with possibly a little stimulant, is prescribed; the action of the bowels should be attended to in conjunction with some of the local means of treatment about to be described, and the disease will get well in a few days.

In severer cases more active treatment is required, and, the disease being essentially adynamic, no lowering methods must be adopted. The diet must be chiefly fluid, milk, eggs, and the like, with a liberal allowance of stimulants. If vomiting be present it may be met by effervescing mixtures or bismuth, and the regular action of the bowels must be ensured. The worst cases require a very large amount of stimulants; and carbonate of ammonia and strychnine may be prescribed in addition. Should the temperature remain persistently high, or hyperpyrexia be present, the effect of large doses of quinine may be tried; but as a rule tepid sponging or the cold bath will prove a more efficient method of treatment. Other antipyretics are less to be trusted, and have too great a tendency to depress the patient. For great restlessness, want of sleep, or delirium, sponging may be employed, or an ice-bag applied to the head. If these fail, morphine is probably the best drug to use, or bromides with chloral may be given.

In addition to the above symptomatic treatment two drugs may be mentioned, which at different times have been considered to act almost as specifics. Of these the best known is perchloride of iron, which is given in very large doses (♏ 40-60 of the tincture) every four hours. The drug is certainly well tolerated in these cases, and probably does good. The other drug is camphor, recommended by Strümpel, but this is of more doubtful value. Camphor is given in three-grain doses every two or three hours, and at the same time the patient is encouraged to drink large quantities of hot tea, so that he soon perspires freely. Quinine was also at one time considered a specific.

An antistreptococcic serum is now prepared from the cocci of erysipelas, and its use has apparently been followed by good results in some cases. To be of value large and frequently repeated injections must apparently be made. It would only be required in the severer forms of the disease; the common mild variety gets well of itself.

Numerous methods of local treatment have been recommended at various times, the very number showing their general inefficiency. It is probable that the simplest are the best; such are dusting the affected part with powdered boracic acid, zinc oxide, or a mixture of these with starch, and covering it with a thin layer of cotton wool. This in part

relieves the painful local sensations, is cleanly, and does no harm. For the face, it is a good plan to cut a mask of lint with holes for the mouth, nose, and eyes, and to keep this moist with evaporating lead lotion. This is very soothing, but must never be applied to any part where there is the least tendency to gangrene. Where the pain is great, tinct. opii ($2\frac{1}{2}$ oz. to the pint) may be added to the lotion. These two methods are better than simply dusting the part thickly with flour, or applying plain water dressings. The dry powders are also much better than the various pastes which are sometimes recommended, or than ointments, at least at this stage. Painting the affected part with collodion usually does harm. If there be very great tension in the affected part, or gangrene threaten, free incisions must be made into it at once, and antiseptic fomentations applied.

Formerly it was much the fashion to apply nitrate of silver over the healthy skin—just beyond the spreading margin of the erysipelatous redness—care being taken not to destroy the whole thickness of the skin; it was asserted that in a considerable number of cases the erysipelas came to a standstill when it reached the line so made. Unfortunately, however, it very often crosses at some part or other and spreads on as before. In place of nitrate of silver some surgeons use iodine. At first sight the value of this method of treatment is not very obvious, and many have asserted that in the cases where the disease was arrested at this line they had to do with mere coincidence. From recent work on the pathology of the disease, however, we can see that the plan was not so useless as may appear. As previously mentioned, the erysipelas cocci spread in the lymphatic vessels of the skin, and it has been found that while, on the one hand, when we have to do with an acute, rapidly spreading erysipelas there is very little cellular infiltration in the part, yet on the other hand, when the process is mild, or when it is coming to a standstill, a large number of cells are present forming a barrier against its further progress. Now the application of nitrate of silver to the skin in so strong a solution as to cause slight ulceration will lead to a rapid exudation of leucocytes which may fill up and block the lymphatic vessels of the part; and thus when the cocci in their spread reach that line, they may find their path barred by a collection of leucocytes.

Not very long ago, when the parasitic nature of the disease was first understood, attempts were made to arrest its spread by the injection of weak antiseptic solutions—such as 2 per cent carbolic acid solution, weak perchloride of mercury lotion, etc.—into the healthy skin just beyond the spreading margin. This method proved untrustworthy. More recently, however, it has been improved by Kraske, whose method of treatment is highly spoken of by those who have experience in erysipelas. This plan is to make numerous scarifications in the healthy skin beyond the spreading margin, the scarifications crossing one another and completely surrounding the disease, as did the old nitrate of silver line. In order to carry out this plan efficiently the patient must be placed under an anæsthetic. When the scarification is complete, a steam spray-

producer, containing 1 to 20 carbolic acid, is made to play on the part for some considerable time (an hour or two); it is subsequently dressed with carbolic compresses. I cannot speak personally of this method, as my experience of erysipelas is insufficient.

When the mouth is affected it should be constantly washed out with simple gargles of boracic acid, Condy's fluid, or sanitas; and if the nose be attacked it should be gently syringed with similar solutions. When the disease affects the throat its gravity must be borne in mind, and in spite of opposition on the part of the patient, a considerable amount of fluid nourishment and stimulants must be administered. The pain of swallowing may be considerably mitigated by the simple plan recommended by Mr. Hovell: an attendant standing behind the patient makes firm pressure, during the act of deglutition, over the ears and part of the neck below by the palms of the hands, the fingers being directed upwards. Locally the patient may be directed to suck ice constantly, and to use weak antiseptic gargles frequently. Sometimes, on the other hand, frequent gargling with a hot saturated solution of bicarbonate of sodium will give most relief. and at the same time hot fomentations may be applied around the angles of the jaw. If these measures fail, free scarification of the palate, and especially of the uvula, will always afford relief. When the larynx is attacked the special danger of suffocation is added, and treatment must be mainly directed to prevent this. All food must be given cold, and all hot or steam inhalations scrupulously avoided. Formerly great reliance was placed on leeches, six to twelve being applied over the larynx, and they certainly give temporary relief. But their tendency is to exhaust the resources of the patient, and usually they have to be repeated. Other means of counter-irritation are useless. The best plan of all is to keep the patient constantly sucking ice; at the same time he should keep quite quiet, and avoid all use of the voice. In some cases this treatment will be all that is required. Where, however, in spite of this the swelling increases, we must either perform tracheotomy or freely scarify the larynx. The effect of the latter may be first tried in adults, where the patient is not too intolerant of the necessary manipulations, and where the dyspnœa is not so extreme as to render the method dangerous from the reflex spasm it excites. The method recommended is as follows:—cocaine is not used, its application wearies the patient, excites spasm, and does no good—guided by the laryngoscope a long, deep incision is made into each aryepiglottic fold, most efficiently by an open knife like Heryng's, rather than by a guarded instrument like Mackenzie's scarifier; it is better to make the incisions into the outer side of these folds, so that the blood may have less tendency to trickle into the larynx, and thus cause much discomfort or even serious danger to the patient. The bleeding is promoted by gargling with hot fluids, and afterwards the patient continues to suck ice.

If this fail to relieve the dyspnœa, tracheotomy will be required, and this should be done as soon as its necessity is foreseen, so as to give the patient his best chance of recovery. Where scarification is out of the

question, as in children and adults who cannot tolerate the necessary manipulations, tracheotomy offers the sole hope of relief; for all other methods of scarifying—by the finger-nail, or by a guarded bistoury guided by the finger-touch—are to be strongly condemned as unscientific and dangerous.

When the parts around the vulva or anus are attacked much relief may be obtained by immersing the child's body in a warm bath to which small quantities of tincture of iodine may be added. The child is slung in a sheet and properly supported, and may be allowed to remain in the bath twenty-four to forty-eight hours at a time.

Finally, in addition to the general and local treatment above described, the presence of complications must be carefully sought or watched for, and especially must the state of the kidneys be investigated, and appropriate treatment adopted in the respective cases.

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INFECTIVE ENDOCARDITIS

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SYNONYMS.—Ulcerative Endocarditis, Malignant Endocarditis, Arterial Pyæmia, Mycosis Endocardii.

Acute endocarditis is to be regarded as a local bacterial lesion occurring as a complication in the course of some general septicæmia, and of the two forms which have long been distinguished—the simple, benign, or verrucose, and the malignant or ulcerative endocarditis—there now is abundant evidence that they represent but different degrees of one and the same morbid process. Acute endocarditis, it would appear from recent investigations, particularly of the more benign cases, is always of microbic origin, and the variability of the type which it may assume seems to depend upon the degree of virulence of the infecting bacteria, rather than upon their kind, and upon the resisting powers of the infected tissues. It thus happens that any one species of organism may be associated with very diverse types of endocardial lesion, and that such conditions as lead to a diminution in the general resisting powers of the organism, or locally of the endocardial tissues themselves, are factors of primary importance in the origin of the more severe or malignant types.

Various names have been suggested for these severe types, none of which, however, is quite unobjectionable: ulcerative and malignant endocarditis are those now most frequently used. Against the name ulcerative endocarditis it may be urged that occasionally no distinct ulcerations are found; whilst on the other hand the ulceration which may result from degenerative changes in chronic endocarditis or in the arteriosclerotic form—the so-called atheromatous ulceration—is not associated with the symptoms of malignant endocarditis. Against the name malignant endocarditis it may be urged that some cases recover; and again, that even the verrucose form may sometimes run a rapid and fatal course (36).

Infectious or infective endocarditis (E. infectieuse, E. infectante, E. végétante of French authors) also is scarcely less objectionable, as with the discovery of organisms in the rheumatic forms of the lesion, they also must be placed in such a category.

As there is now clear proof that malignant endocarditis is of bacterial origin, and that it is but a local complication occurring most commonly in septic and pyæmic diseases, we think that the proper place for infective endocarditis is amongst the infective diseases.

History and Etiology of the Disease.—Bouillaud (1824-1832) is said to have been the first to indicate a form of acute endocarditis which occasionally began with pyæmic symptoms; but he did not recognise the relation of the endocardial lesions to the general symptoms: Stenhouse Kirkes (1853) was the first to comprehend the malignant form of endocarditis: he looked upon the general or typhoid symptoms as due to an

altered condition of the blood produced by the granular masses detached from the diseased valves. Virchow not only pointed out the embolic nature of the blocks found in the small arteries in cases of valvular lesions of the heart, but, in a case of puerperal perimetritis, with peritonitis and diphtheritic deposits in the large intestines, he also described coagula with granular masses, like diphtheritic deposits, on the mitral valve; and he looked upon the process as possibly due to a parasitic cause.

The pyæmic character of malignant endocarditis was also early noted by Sir S. Wilks, who afterwards suggested the name of arterial pyæmia for this affection; he was followed by J. W. Ogle, Murchison, Moxon, Bristowe, and other English writers. Bamberger and Friedreich laid stress on the similarity of the symptoms in some forms of endocarditis and in pyæmia; and of the early French observers we may note Charcot and Vulpian, and Lancereaux, who described the clinical characters of malignant endocarditis. Not a few observers, such as Hayem and Dugues, and Desplats, looked upon the valvular lesions and the lesions in the other organs as local manifestations of a general infectious disease.

Rokitansky (1855) was apparently the first to indicate the presence of bacteria in the endocardial lesions. Winge also described microbes (which he spoke of as chains of small rods or round granules like chains of leptothrix) both on the valves and in the secondary infarcts in a case of infective endocarditis; and, as the patient had suffered from suppuration of a toe, he thought the microbes, which he regarded as the cause of the disease, were derived from this source: he accordingly proposed for the disease the name mycosis endocardii.

Heiberg found bacteria similar in character to those seen by Winge in a case of infective endocarditis in a puerperal case. He inserted particles from the affected valves into the peritoneal cavity of a rabbit, but with negative results. Nevertheless Heiberg's observations formed the starting-point of a series of similar publications, all of which made for the existence of microbes in the diseased valves: some of the cases, like that of R. Meier, were primary infective endocarditis; in others (Wedel), the primary source was septic endometritis, whilst in others again (34), the primary disease was pneumonia with empyema.

Birch-Hirschfeld not only found numerous micrococci, in zoogl\u0153a-masses and in chains, in the diseased valves, and in the metastatic infarcts, but he also succeeded in producing panophthalmitis in three rabbits by inoculation with fragments from the valvular deposit. Klebs made some important contributions to this subject: from an examination of twenty-seven cases of endocarditis he came to the conclusion that all forms of this malady are of mycotic nature; the verrucose form being due to cocci (monadines), the other (which he calls the septic endocarditis) to a somewhat different organism (a capsulated coccus). Köster, by a series of observations, confirmed the opinion of Klebs that every endocarditis, whether malignant or benign, is caused by bacteria; finding, moreover, that many of the vessels of the affected valves were filled with thrombi consisting of cocci, he came to the conclusion that the endocar-

ditis was produced by these microbic emboli which rupture the walls of the vessel and reach the free surface of the valve. About this time Dr. Cayley, who suggested the name infecting endocarditis, and Professor Purser published malignant cases of endocarditis, in which they described the presence of bacteria. Litten confirmed the observations of Klebs and Köster. In the meantime the clinical features of infective endocarditis, and its relation to the simple or rheumatic endocarditis, were made the subject of further study by many pathologists and clinicians, some of whom will be referred to in the clinical section; at present I will mention only the papers by Dr. Goodhart and Professor Osler.

With the progress of bacteriology, our knowledge of the organisms found in this disease has become more definite; pure cultures of them have been obtained, and their behaviour when injected into animals definitely followed. A series of important observations was published between the years 1885 and 1888, amongst others by the following observers:—Wyssokowitsch, Cornil and Babes, Ribbert, Senger, Bramwell, Netter, Prudden, E. Fränkel and Sänger, Stern and Hirschler, Weichselbaum, Dreschfeld, O. Rosenbach. Of the papers treating on the etiology of this disease published since 1888 I may cite those of F. Taylor, Gilbert and Lion, G. Lion, Roux and Josseraud, and Dessy.

If we summarise the results of these and some other observations we arrive at the following data:—

1. That in nearly all the cases of infective endocarditis, whether ulcerative or not, bacteria were found.

2. That in most cases only one organism was found, but in a few (Weichselbaum, Stern, Hirschler, Fränkel, etc.) more than one.

3. That the organism found was not the same in all. In many cases an organism was found which occurs in other infective diseases, whilst in some an organism occurred not hitherto found in other diseases.

The organisms belonging to the first group were: the streptococcus pyogenes (including the streptococcus of erysipelas); the staphylococcus pyogenes aureus, the staphylococcus pyogenes albus; the pneumococcus of Fränkel and the pneumobacillus of Friedländer; the diplococcus of Weichselbaum; the typhoid bacillus (20); the bacillus coli communis; the bacillus of tuberculosis (10, 25, 32); the bacillus of diphtheria (26); the gonococcus (36, 59*a*); the bacillus pyocyaneus; the micrococcus rheumaticus.

The organisms belonging to the second group were bacillus endocarditidis griseus (Weichselbaum and Netter); micrococcus endocarditidis rugatus (Weichselbaum); bacillus endocarditidis capsulatus (Weichselbaum); bacillus immobilis et fœtidus (Fränkel and Sänger), and the bacillus of Gilbert and Lion; the coccus of Josseraud and Roux; the micrococcus tetragenus citreus of Sterling; the micrococcus zymogenes of MacCallum and Hastings (besides a few others with less definite specific characters).

4. In most cases the organism found in the diseased valves was also met with in such secondary deposits as infarcts and metastatic abscesses.

5. The organisms most frequently found were the streptococcus pyogenes, the staphylococcus pyogenes aureus, and the pneumococcus. The first two were found chiefly in cases in which the endocarditis was primary, in cases of puerperal diseases, of pyæmia and septicæmia (wounds, abscesses, osteomyelitis, etc.), and especially in those cases in which the infective endocarditis had attacked valves already affected with chronic rheumatic endocarditis.

The pneumococcus has been found mostly in cases where croupous pneumonia was present, and in some of meningitis without pneumonia. As streptococci and staphylococci have also been found in the affected valves when the primary disease was enteric fever, diphtheria, gonorrhœa, and so forth, it is evident that sometimes the endocarditis is due to a mixed infection.

6. Experimental investigations on animals have led to diverse results. Particles of the diseased valves inserted into the subcutaneous tissue, into the peritoneal cavity, or into the anterior chamber of the eye, have sometimes produced no effect; but often they have given rise to local abscesses. Injections of pure cultivations into the peritoneum or under the skin sometimes produced no results; at other times they gave rise to marked septic symptoms and lesions.

Endocarditic lesions have been produced by the injection into animals (most frequently rabbits and dogs) of pure cultivations of the organisms found on the diseased valves in cases of malignant endocarditis. Some observers—Ribbert, Perret and Rodet, Bonome, Dreschfeld, Mannaberg, Gilbert and Lion, Roux and Josseraud, and Vaillard—by injecting pure cultivations into the jugular vein of rabbits, succeeded, without previously injuring the valves, in producing inflammatory changes, with or without ulceration, in the aortic valves, and often also in the mitral and tricuspid valves; and in the valvular deposits masses of the organisms of the pure culture were found both on the surface, in the deeper layers of the deposits, and, in some few cases also, inside the capillaries and small arteries of the inflamed valves. Other changes found in the animals experimented upon were:—Enlargement of the spleen, metastatic infarcts, and hæmorrhage into the brain. These various lesions, though evidently the result of the microbes, were, however, by no means uniformly found. Gilbert and Lion, by the injection of a peculiar bacillus found in a case of infective endocarditis into a vein of the ear in rabbits, produced marked endocarditis with many secondary changes (softening and hæmorrhages in the central nervous system).

The majority of experimenters, however (Rosenbach, Orth, Fränkel and Sänger, Weichselbaum, etc.), only succeeded in producing endocarditis when the aortic valves had been injured shortly before injecting the cultures into the jugular vein. The aortic valves were injured by introducing a sterilised stylet through the carotid into the left ventricle, a method first made use of by Rosenbach. Secondary or metastatic changes of bacterial origin were also found in these animals, together with other lesions, such as enlargement of the spleen, fibrinous pleurisy.

7. The examination during life of the blood of persons suffering from infective endocarditis has shown in a few cases, especially on the application of certain methods which will be given in the clinical section, the presence of bacteria of the pyogenetic kind.

As regards the nature of infective endocarditis the conclusions which we may draw from the above data are :—

(i.) Infective endocarditis is a bacterial lesion occurring as a local complication in some general infection.

(ii.) It is not a pathological entity, since it is produced by several distinct species of bacteria, either separately or together.

(iii.) The organisms most frequently associated with this lesion belong to the septic and pyogenetic types (streptococci and staphylococci).

(iv.) Of other organisms, the diplococcus of pneumonia often gives rise to infective endocarditis; the specific organisms of typhoid fever, gonorrhœa, diphtheria, tuberculosis do so very rarely: infective endocarditis occurring in the course of any one of these affections, or found in valves already the seat of chronic endocarditis or atheroma, is due to septic organisms, and must be looked upon as the sequel of a mixed infection complicating these diseases.

(v.) Valves weakened or altered by disease are more frequently the seat of infective endocarditis.

(vi.) Bacteria which have been found to be the cause of malignant endocarditis have under other conditions been found to be associated with the non-malignant or verrucose endocarditis.

Etiologically we may distinguish the following types of infective endocarditis :—

(*a*) Primary infective endocarditis.

(*b*) Infective endocarditis as a complication of septic disease (pyæmia, septicæmia, puerperal affections, gonorrhœa, traumatism).

(*c*) Infective endocarditis as a complication of pneumonia or meningitis, and due to the diplococcus pneumoniæ.

(*d*) Infective endocarditis as a mixed infection due to septic organisms secondary to acute infectious fevers, or secondary to rheumatic endocarditis or sclerotic conditions of the valves.

Remote Causes.—1. A debilitated state of the system. Though infective endocarditis occasionally attacks persons of sound constitution and in good health, it is more often noticed in debilitated persons, in drunkards, in persons suffering from nervous depression and the like, or suffering from such chronic exhausting diseases as cirrhosis of the liver (57), or from symptomatic anæmia, or chlorosis.

2. The presence of an infectious disease. This point need scarcely be dwelt upon again. Besides the various affections, septic and non-septic, already mentioned, we may note also dysentery, malaria, small-pox, scarlet fever, epidemic influenza (Fiessinger) as diseases which, by lessening the resistance of the body, favour the entrance and growth of the pyogenetic organisms. Syphilis does not appear to enter into the causation, and the endocarditis accompanying it

is more of a sclerotic and fibrous nature with fibrous changes in the myocardium.

3. During pregnancy and the puerperal state infective endocarditis has repeatedly been observed, especially in the presence of a septic or pyæmic affection of the uterus or its appendages.

4. Chronic valvular affection of the heart, the result of chronic endocarditis or produced by sclerotic changes, commonly enters into the causation. The frequency of previous valvular lesions is given by Dr. Coupland as 61 out of 69 cases, 75 per cent by Professor Osler, 65 per cent by Kanthack and Tickell, 59 per cent by Washbourn, 83 per cent by Dr. Glynn, whilst in 45 cases met with in the Manchester Royal Infirmary there was evidence of old endocarditis in 77 per cent.

5. Gall-stones, with or without suppuration in the biliary passages, have occasionally been known to give rise to infective endocarditis. As yet seven cases only have been published, but I may mention another which occurred in a patient under the care of my colleague Dr. Steell. Murchison noticed this association in his work on *Diseases of the Liver*, and other cases have been described by Jaccoud, by Mathieu and Malibran, by Netter and Martha, and more recently by Leva, who gives the literature on this subject. Netter and Martha found a small bacillus in the biliary abscesses, and also in the endocarditic deposits. As the bacterium coli commune is occasionally found in calculous affections of the biliary apparatus, the connexion between cholelithiasis and infective endocarditis, even when there is no suppuration, is easily understood.

6. That chorea, which is so closely connected with rheumatic endocarditis, may be associated with infective endocarditis, is shown by the following case which was under my care in the Manchester Infirmary. A boy, aged eleven, suffering from chorea; there was no history of rheumatism, and, on admission, no sign of endocarditis. A week after admission he began to be feverish, and a loud mitral systolic bruit appeared; a fortnight later he showed signs of a cerebral affection (severe headache, delirium, optic neuritis, hemiparesis). At the post-mortem examination infective endocarditis of recent date and a small abscess of the brain with suppurative meningitis were found. The valves showed no signs of chronic disease. Barkley (47) gives a case of chorea, terminating fatally, in which endocarditis, abscess of the parotid, and bronchopneumonia were found; the endocarditis in this case may possibly have been secondary to the pneumonia.

7. Traumatism, apart from external wounds and injuries, may give rise to infective endocarditis in another way, namely, by an injury causing rupture of a heart valve. Biggs gives a case in which the aortic valves were ruptured by a fall, and infective endocarditis supervened. A similar and very interesting case came under my notice. A gentleman, a patient of Dr. Stott of Haslingden, had been under observation for several years on account of slight albuminuria, for which he periodically consulted the late Sir William Roberts. He met with a

severe bodily strain, and shortly afterwards, not feeling well, consulted Sir William Roberts again, who then for the first time detected a loud aortic diastolic bruit. He returned to Haslingden, and, some short time after, he began to suffer from symptoms of malignant endocarditis (repeated rigors, which recurred almost daily, intermittent pyrexia in which the temperature rose to 105° F., and eventually embolism of the posterior tibial artery): from this state after a time he recovered to enjoy good health, though the loud diastolic aortic bruit persisted.

8. Climatic conditions appear to me to have some influence in this matter. I have noticed that cases of infective endocarditis occur more frequently during the autumn; and in several cases the patient before the attack had spent some time in a swampy or marshy district. Decaying vegetable matter may have something to do with the outbreak of the disease in these cases.

9. Infective endocarditis occurs especially between the ages of 20 and 40. It is very rare in older people, and, according to Professor Osler, it is also very rare in children (3 or 4 out of 209 collected cases). From my own observations infective endocarditis in children would appear not to be so rare as this estimate would indicate. Men are more frequently affected than women [62 per cent of Osler's, 65 per cent of Glynn's cases].

The paths of entrance of the microbes, as in other septic diseases, vary in the different groups of cases. We may notice as the chief portals :—

(*a*) The skin and subcutaneous tissue. Many of the septic cases, following abrasion or ulceration of the skin, belong to this group; and likewise the cases of infective endocarditis following boils, carbuncles, gangrene, erysipelas, and the like. Considering how slight an abrasion may sometimes be followed by septic infection, it is possible that in some cases of the so-called "primary" infective endocarditis the germs may have entered the system in this way.

(*b*) The osseous system, as in osteomyelitis and otitis media.

(*c*) The mucous membranes of the digestive tract. Ulceration of the intestines explains the occurrence of infective endocarditis after enteric fever and dysentery. In several of the recorded cases, besides the ulceration in the intestines, there was an old lesion of the valves. Gangrenous stomatitis, glossitis, and ulcers on the tongue and lip are occasionally quoted (Brissaud, Gilbert) as primary channels of entrance. Probably the tonsils, which are so often affected in rheumatic endocarditis, may occasionally serve as the means of entrance, and thus again some of the so-called "primary cases" may be explained.

(*d*) Of the biliary passages we have already spoken.

(*e*) The genito-urinary organs. The frequent occurrence of infective endocarditis in puerperal disease and after abortions has been noted; the channels along which the infection travels are the uterine lymphatics and veins. In men the mucous membrane of the urinary tract may form the starting-point, as in gonorrhœa, or bladder and kidney affections, which have sometimes been followed by infective endocarditis.

(*f*) Respiratory tract. We know that many infective germs may pass into the blood through the respiratory passages, often after having caused such changes in the epithelium as facilitate their entrance into the blood. But it may also be admitted that germs may pass through the lungs, and find their way into the circulation without any previous injury, and so give origin to an apparently primary infective endocarditis. Buchner has demonstrated that certain organisms can pass through the pulmonary epithelium without the intervention of any mechanical lesion, and may then enter the circulation through the lymphatics. Viti states that he has actually produced infective endocarditis in animals by the introduction of bacteria into the lungs.

The frequent association of infective endocarditis with pneumonia need scarcely be mentioned again: the disease has also been noted in bronchiectasis by Thiroloix. The microbes, having reached the blood, find access to the valves either on their free surface by deposition from the circulating blood—a view set forth by Virchow—or by way of the vessels of the valves in which they form small emboli, and thence penetrate into the tissue and to the surface—a view already attributed to Köster. Most observers are inclined to adopt Virchow's opinion, one strongly supported by experimental pathology (seeing that infective endocarditis so often attacks valves already diseased), and by arguments based upon the paucity of blood-vessels and capillaries in the valves even when inflamed. On studying the distribution of the micro-organisms in sections of the diseased valves, I have been struck by the gradual diminution in their number from the surface of the valve inwards; but this may well be due to the more favourable conditions on the surface of the valve for their growth.

Several observers, however (Cornil and Babes, Köster and others), have described numerous emboli, consisting almost entirely of microbes in the vessels of the inflamed valves. There is no reason why we should not accept both these views, admitting the possibility of an embolic origin only in the case of valves which have become vascularised in consequence of the organisation of a previous inflammatory lesion (chronic endocarditis).

Chemical Pathology.—On this subject, which is sure to become an important one in all bacteriological diseases, we have to record the observations of Dr. Sidney Martin, who, in connexion with his important researches on diphtheria, studied the action of the chemical poisons in infective endocarditis and in anthrax. A chemical examination of the blood and of the spleen (by his method) from a case of infective endocarditis, in which a staphylococcus, which could be cultivated, was found in the diseased valves, showed the presence of two bodies—a proteid (proto- and deutero-albumose) and a non-proteid product of strong acid reaction. The albumoses when injected into animals produced fever, and retarded the coagulation of the blood; and the fever increased with the quantity injected: the albumoses from anthrax were more toxic, and caused greater loss of weight in the animal. The post-mortem examina-

tion of the animals that died, or were killed, showed that no pathogenetic organism was present; when a large single dose of the albumoses was injected into the animal fatty degeneration of the heart was found after death.

Pathological Anatomy.—The anatomical changes met with in infective endocarditis are those of the primary septicæmia, those in the heart due to implication of the endocardium, and those secondary to the endocardial changes, namely, various lesions of embolic origin. The lesions which may be regarded as the starting-point of, or as immediately correlated with, the primary infection of the blood-stream have already been indicated. Pneumonia, empyema, phthisis, gonorrhœa, and various septic processes may be clearly primary: in many cases, however, the precise significance of such lesions as pneumonia, meningitis, empyema, and localised suppuration in other situations is more difficult to determine, since they may be secondary to the endocardial lesions. Among the general manifestations of the septicæmia or septico-toxæmia certain changes are constantly present, as cloudy-swelling and fatty degeneration of the parenchymatous elements of the glandular organs, especially the liver and kidneys, and of the heart-muscle; enlargement of the spleen, generally to three or four times its average weight, with softening of its pulp; and occasionally a pronounced nephritis of a hæmorrhagic character. In the heart the endocardial lesions present considerable variability expressive of the virulence of the infecting organism and of the resistance of the tissues. Like the less severe varieties of endocarditis, the infective form principally affects the valves; and much more frequently the valves of the left side than those of the right, though the latter are more liable to be affected than in rheumatic endocarditis: thence it may extend to other portions of the endocardium, and to the aorta or pulmonary artery. Mural infective endocarditis, in which the valves remain free, is extremely rare.

When there are only vegetations these are generally small, and greyish or yellowish in colour; they affect the base as well as the margins of the valve. Such a condition is sometimes seen in cases which run a very rapid course; histological examination of the valve reveals numerous bacteria, proliferating connective-tissue cells, and leucocytes, besides the layers of fibrin. In most cases, however, the vegetations are larger, occasionally pedunculated, and more or less extensively ulcerated; these may be superficial, not extending deeply into the tissues; they are greyish, and often partly covered with fine blood-coagula; if the valve yield to the blood-pressure, depressions (aneurysms) may result. Sometimes the ulceration may penetrate deeply into the valve, and perforate it; often the inflammation spreads to the chordæ tendineæ, and is followed by further ulceration, so as to cause detachment of the valve segment; the valve is thus rendered incompetent, and with every cardiac contraction the loose segment, flapping against a part of the auricle, sets up fresh inflammation there, and gives rise to the formation of warty

growths on its walls. The loss of substance caused by ulceration extending to parts of the endocardium (chordæ tendineæ, septum) may lead to an aneurysmal bulging of the wall, or even to rupture of the septum or of the heart.

It is said that when streptococci are the immediate cause of the ulcerative endocarditis the lesion tends to assume a hæmorrhagic type, with staphylococci small abscesses may form in the tissues of the valves, and that with the pneumococcus the lesion is peculiar by reason of the exuberance of the vegetations. Abscesses may be found in other parts of the heart, extending deep into the myocardium; and these again may lead to an aneurysm of the heart, or to rupture into the pericardium. In rare cases the pus may be reabsorbed, and leave scars or calcareous residues (71).

In the more chronic, and sometimes even in the acute cases, we may find deposits of lime salts in the vegetations; but, as a rule, these calcareous incrustations occur in cases in which ulcerative endocarditis has attacked a person already suffering from valvular disease. It is not always easy to distinguish these ulcerations from the atheromatous ulcers due to simple necrosis in a valve with calcareous deposits, the result of either chronic endocarditis or atheroma; in most cases a bacteriological examination will help to distinguish the two, but not always.

The frequency with which the various valves are affected is shown by combining the statistics of Osler, Washbourn, and Glynn (total number, 356 cases):—

Mitral.	Aortic.	Mitral and Aortic.	Tricuspid.	Pulmonary.
130	79	94	32	22

In sixteen cases the right side of the heart alone was affected.

Lesions due to embolism. These vary as the embolus acts mechanically or has pyogenetic properties: in the first case we meet with simple infarcts chiefly in the spleen and the kidney, and in the brain; in the brain the area of the blocked artery softens, in the peripheral arteries the embolus may lead to gangrene. In the second case we meet with metastatic abscesses, which may occur either in small or in very large numbers; and are found in the liver, the spleen, the kidney, the lungs (especially if there be right-sided endocarditis). In the intestines, and even in the stomach, hæmorrhagic infarcts are found, sometimes of a septic nature infested with numerous micro-organisms, and occasionally leading to ulceration of the mucous surface; at other times corresponding to simple infarcts, the intestines present intense congestion, hæmorrhage, and even gangrene. Small capillary emboli are no doubt the cause of the hæmorrhages noted in the skin and subcutaneous tissue, the serous surfaces, the retina, and other parts. In sixty-four cases Dr. Glynn found infarcts in the lungs in seven, in the spleen in thirty, in the kidneys in twenty-five, and in the brain in twelve.

Symptoms.—The symptoms of infective endocarditis vary considerably in individual cases: the heart symptoms may be quite insignificant or even absent; as, for example, when acute infective endocarditis complicates a septic disease, as pneumonia, empyema, or meningitis, in which often only the autopsy reveals the endocardial lesions. In other cases the heart symptoms are more pronounced: this is more particularly the case in the subacute or even chronic form which complicates rheumatic endocarditis. Owing to the great diversity of the symptoms, certain types of infective endocarditis have been formulated. We may distinguish in the first place between an acute form and a subacute or chronic form.

The acute form includes the septic type, the typhoid type, and the cerebral type; the chronic form is noticed in old valvular affections of the heart; by some it is called the cardiac type, or, owing to the peculiar fever curve which is noticed, it has been named the intermittent febrile or malarial type. We will briefly consider the principal features of these various types, and then note the symptoms in detail.

(*a*) The *septic or pyæmic type*, which is noticed in puerperal cases and in other forms of septicæmia and pyæmia, includes all the symptoms of a severe septic infection. The onset is acute; with or without preceding general malaise, the disease is ushered in by more or less severe rigors, followed by heat and sweating, which may be repeated after a shorter or longer interval; between the rigors the temperature generally remains high, it may, however, be remittent; the skin may show patches of erythema, hæmorrhage, or superficial collections of pus; the pulse is quick and feeble; the respiration is hurried and superficial; nervous symptoms, such as headache, delirium, somnolence, are usually present; at times symptoms of cerebral embolism may appear; the tongue is usually furred, and may become dry and brown; there may be great thirst, anorexia, and vomiting; there is often a good deal of tympanites and diarrhœa. Metastatic abscesses may form in various organs and tissues, but often do not give rise to definite symptoms, as, for example, in the lungs. The examination of the heart may reveal either no abnormal signs, or audible murmurs; from their presence alone we may not conclude that we have to do with infective endocarditis, for such murmurs are not uncommon in simple cases of pyæmia and septicæmia, without any ulceration of the valves of the heart. Of other symptoms common in ordinary pyæmia I may mention albuminuria, jaundice, and pain and swelling of the joints with suppuration. Death generally takes place within one or two weeks.

(*b*) In the *typhoid type* infective endocarditis resembles enteric fever as regards the general aspect of the patient, the condition of the tongue, which is brown, dry, and furred, the presence of diarrhœa and cerebral symptoms; but we not infrequently see rigors, petechiæ, and optic neuritis—symptoms which are very rare in enteric fever: the heart symptoms in this form again may be absent or indefinite. The temperature

is generally very irregular; rigors may occur throughout the whole duration of the disease, followed by profuse sweating; and attacks of embolism in the brain, kidney, and spleen are not uncommon. The duration of the disease, when assuming this form, varies from two to three weeks; sometimes it lasts longer.

(*c*) *Cerebral type.*—This type is chiefly abstracted from cases of malignant endocarditis complicated with meningitis, either cerebral or cerebrospinal. The affection begins in these cases with cerebral symptoms—headache, somnolence going on to unconsciousness and coma, or delirium and convulsions. The heart symptoms are less pronounced and often absent. Rigors are not often present, but attacks of embolism may occur and direct attention to the heart.

(*d*) *Cardiac or Malarial type.*—This represents by far the largest number of cases; it occurs in persons in whom the heart has already been damaged by previous disease. It runs, as a rule, a subacute and chronic course, and may last six months, or even more than a year. Though recovery is extremely rare, this variety is not always fatal.

The onset of the disease is generally insidious; the patient complains of general malaise, and has an anæmic appearance. Sometimes a raised temperature, with but few symptoms, may be the first sign of it, as in a case under the care of my colleague Dr. Steell: a young man suffering from an old valvular affection of the heart, whilst in the hospital suddenly showed a rise in temperature, and after a few days manifested characteristic signs (rigors and so forth) of infective endocarditis. At other times the affection resembles rheumatic synovitis, pains in the joints and slight pyrexia being prominent features. After these symptoms have lasted a few days, rigors appear, followed by heat and sweating. During rigor the temperature may reach 104° F. or more, and a few hours later the temperature may come down to normal. The rigors occur at irregular intervals: two or three may occur in one day; at other times several days or weeks may elapse before a second rigor is observed. In a good many cases the rigor is replaced by a mere sense of chilliness followed by sweatings; in others, again, a remittent or intermittent pyrexia, going on for weeks or months without any rigors, is a prominent feature. Thus, in one case, which I saw with the late Dr. Renaud—a girl, aged 20, who at the age of 16 had had an attack of rheumatic fever, leaving her with mitral disease—the only noticeable feature was an intermittent pyrexia—the morning temperature being 98° F., the evening temperature 99° to 100°; beyond this no other symptom was noticed, and the patient felt no further inconvenience. This state persisted for over six months, when she had an attack of cerebral embolism. From this she had partially recovered when a second and fatal attack of embolism supervened. At the necropsy recent vegetations upon an old affection of the mitral valve showed the presence of numerous streptococci.

A remarkable feature in the cardiac type of infective endocarditis is the occurrence of embolism. This occasionally affects peripheral arteries

(posterior tibial, brachial, popliteal, and even the abdominal aorta), but more often the left middle cerebral artery, or one of its branches, especially the Sylvian artery. The blocking of the cerebral vessels may only produce temporary paralysis or aphasia; but often these attacks are followed by others which leave permanent results, and most frequently lead to complete hemiplegia.

Some of the viscera also may be the seat of emboli; thus *splenic infarcts* are not uncommon, and may give rise to no symptoms; but occasionally certain symptoms enable us to diagnose the infarction; namely, sudden pain in the region of the spleen, with enlargement of the organ, and occasionally a friction sound over the spleen. It must not be forgotten, however, that, without the presence of an infarct, the spleen is often considerably enlarged in infective endocarditis.

Quite as common are *renal infarcts*, which only give rise to symptoms when the infarct is large; in such a case sudden pain is felt in the region of the kidney, and hæmaturia and remittent pyrexia appear.

Infarcts of the lungs can be inferred if the patient have a sudden pain in the chest, with dyspnœa, followed by the expectoration of sanguinolent sputum. On physical examination, if the infarct be large, we notice over a small area dulness on percussion, increased vocal fremitus, bronchial or tubular breathing, and fine crepitations; the temperature also rises and assumes a remittent character. Pulmonary infarcts frequently lead to embolic pneumonia, and often also set up localised pleurisy. If the endocarditis be situated on the right side of the heart, we occasionally meet with multiple metastatic abscesses in the lungs, which give rise to no definite symptoms.

Embolism of the mesenteric artery—a rare occurrence—may give rise to severe abdominal pain, with hæmorrhage from the bowels and grave general disturbance leading to collapse.

Other symptoms often noticed are pronounced anæmia, which may be present from the beginning: examination of blood shows the red blood corpuscles to be diminished; the leucocytes are often increased, and a few eosinophil cells may be detected. Bacteriological examination of the blood may reveal the presence of micro-organisms, notably streptococci.

Petechiæ and hæmorrhage from the mucous membranes are occasionally noted, the latter more particularly when the aortic valves are affected.

Pains in the joints are often complained of; in many cases the joint is neither swollen nor reddened, and the affection is probably of a toxic nature; at other times we meet with a definite arthritis, or again, with suppuration of the joint.

Hæmorrhages in the retina and *optic neuritis*, according to some observers, are of common occurrence. I have seen hæmorrhage more frequently than optic neuritis.

Enlargement of the spleen is very often noticed, and may reach a considerable degree, so that the organ can readily be felt; it is not a

constant sign, however, and in some cases the spleen, as shown by the necropsy, is even smaller than in the normal state.

The *liver* is sometimes found enlarged, and jaundice may be present. In rare instances the liver appears diminished, and the case may simulate acute yellow atrophy. The occurrence of infective endocarditis in persons suffering from gall-stones has already been alluded to when speaking of the pathology of the disease; this may occur in persons who have not had rheumatic endocarditis.

The *urine* often shows traces of albumin and blood, and the presence of casts, both epithelial and granular.

The *bowels* are often constipated; occasionally we meet with profuse diarrhœa, and sometimes (see above) with hæmorrhage from the bowel.

The ordinary *complications* are pneumonia, pleurisy, pericarditis, aneurysm, cerebral hæmorrhage; this last was noticed in two cases which occurred in the Manchester Infirmary; an embolus was carefully searched for, but with negative results.

The symptoms which relate to the heart are well pronounced in the cardiac form, and we meet with the signs of mitral or aortic disease, or of both; in rare cases there is evidence of an affection of the valves of the right side of the heart. There is nothing in the character of the bruits or in the size of the heart to enable us to diagnose infective rather than benign endocarditis; during the course of the disease the murmur may undergo some change, but this may also occur in rheumatic endocarditis. The presence of right-sided valvulitis is of greater diagnostic value, as it is of very rare occurrence in the rheumatic or benign endocarditis. Some authors lay stress on the loudness of the murmurs, on their peculiar (metallic) character, and on the propagation of the mitral murmur to the axilla and angle of scapula; but these signs are also noticed in the benign form of endocarditis. The incidence of malignant endocarditis in cases of old valvular disease may lead to sudden and marked alteration in the character of the murmurs. Subjective symptoms, such as palpitation, pain over the region of the heart, excessive dyspnœa, have no diagnostic value.

As already stated, the cardiac form of infective endocarditis almost always runs a chronic course; occasionally it may occur in an acute form. When treating of the pathology, I mentioned one instance in which, previous to the occurrence of infective endocarditis, there probably had been a ruptured aortic valve. I saw, with Mr. Coutts of Blackley, a case of infective endocarditis in a compositor, aged 50, who had always enjoyed good health, and who had never been troubled with rheumatism; he was suddenly seized with a rigor while at his work; he was brought home, and his wife, who had been a nurse, took his temperature and found it 103·5° F.; in the course of a few hours the temperature was again normal, and the patient felt quite well. The morning after, he had another rigor and rise of temperature; and in the evening he had yet another rigor. When I examined the patient soon after, I found the temperature normal, and the patient complaining

only of some oppression; the heart's action was somewhat tumultuous, and the arteries beating rather forcibly; over the aorta a faint systolic bruit was audible. The spleen was enlarged. The patient had been taking quinine, and now some arsenic was added to this; the rigors, however, continued for two days, when the patient suddenly died. I looked upon this case as one of idiopathic acute infective endocarditis.

The above types by no means represent all the clinical forms of infective endocarditis. Thus it is found in association with pneumonia, in which case there is very often no special symptom to lead one to suspect its presence. It may occur with gonorrhœa, in which case the heart symptoms are often pronounced, whilst septic symptoms are less obvious; and, lastly, we meet with cases in which the distinction between rheumatic and infective endocarditis is impossible.

Diagnosis.—In spite of our improved clinical methods, and the application of bacteriology to clinical medicine, the diagnosis of infective endocarditis is still often a matter of difficulty.

Enteric fever may be distinguished from infective endocarditis by the mode of onset, the temperature curve, the roseolar spots, tympanites, and so forth. (See "Enteric Fever," p. 1103.) Repeated rigors are rare in enteric fever, and cardiac murmurs seldom appear at the beginning of it. In doubtful cases the agglutination test may be a useful help; if, after the sixth day of illness, this test give negative results, enteric fever may with great probability be excluded; on the other hand, repeated rigors, and especially the occurrence of attacks of embolism, are in favour of infective endocarditis.

From septic and pyæmic infection, unless heart symptoms are pronounced and signs of embolism are present, the disease is not easily distinguished. This will be easily understood, for infective endocarditis is indeed nothing more or less than a septic disease with the special localisation of the micro-organism in the heart valves. Bacteriological examination of the blood (see p. 920) commonly shows us the presence of septic micro-organisms; and the same observation applies to the meningeal or cerebral form. It is only in cases of tuberculous cerebrospinal meningitis that the withdrawal of fluid by means of puncture of the spinal membrane in the lumbar region—which would show the presence of tubercle bacilli—can be of any diagnostic value; as the same organisms found in non-tuberculous meningitis, be it suppurative or cerebrospinal, have been found in infective endocarditis.

In the cardiac form, when the heart symptoms are well pronounced, several signs help us to distinguish between the rheumatic (or benign) and the malignant endocarditis. These are:—

(i.) *The presence of pyrexia.*—This is often one of the first symptoms, and may show the remittent or intermittent type; should the pyrexia be accompanied by rigors occurring at irregular intervals and not affected by either quinine or arsenic, the diagnosis may be looked upon as almost certain.

(ii.) *The anæmic appearance of the patient.*—Anæmia often follows

the first attack of rheumatic endocarditis; but the persistence of anæmia for a long time, or the occurrence of anæmia long after the attack, should certainly make us suspect malignant endocarditis.

(iii.) Enlargement of the spleen has already been discussed on p. 917.

(iv.) Changes in the retina, whether in the form of optic neuritis or of small hæmorrhages, when occurring in persons suffering from endocarditis, are indicative of the infective form; and it is well to examine the eye in all cases of endocarditis.

(v.) Hæmorrhages in the skin and from the mucous membranes.—Epistaxis is a common symptom in rheumatic endocarditis when the aortic valves are affected; and hæmoptysis is frequently noticed early in mitral disease, and at a later stage in other heart affections. Hæmorrhages into the skin and subcutaneous tissue, on the other hand, due probably to numerous small capillary emboli, are indicative of infective endocarditis. Of hæmaturia from renal infarcts and of melæna from embolism of the mesenteric arteries I have already spoken; but in themselves, and without other signs of infective endocarditis, these hæmorrhages are of no diagnostic value, as they may be the result of the chronic venous congestion secondary to chronic endocarditis.

(vi.) Bacteriological examination of the blood.—Many are the observations on this subject, and various the methods which have been devised to obtain sufficient blood for the culture of micro-organisms (*vide* p. 642.) Petruschky uses the blood obtained by cupping. Lithmann withdraws about 5 c.c. of blood directly from a vein of the arm by means of a sterilised syringe. A portion of this is mixed with agar-agar which has been previously liquefied in a water-bath at a temperature of 40° C., and the mixture is poured out into Petri's capsules to secure cultivations of the micro-organisms present. In the acute septic cases numerous cultures of streptococci and other cocci are found; in the chronic cases, though the case may be one of infective endocarditis, this method does not always show the presence of micro-organisms. Of three chronic cases of infective endocarditis H. Cohn found a few colonies of staphylococci in one only. In several cases of chronic infective endocarditis under my own care, in which the diagnosis was verified by the autopsy, some venous blood was aspirated after the method of Lithmann, and examined bacteriologically by my colleague Professor Delépine, but with negative results.

Prognosis.—The prognosis of this disease is in all cases very grave. The acute form, be it of the pyæmic, typhoid, or meningeal type, is almost invariably fatal, death taking place sometimes within a few days. Eberth gives the case of a man who began with typhoid symptoms, soon followed by coma and hyperpyrexia; the case ended fatally the next day. The aortic valves showed ulcerations, and a metastatic abscess was found in the brain. In other cases the symptoms may go on for several weeks. The chronic or cardiac form may last for months and occasionally over a year; yet a fatal termination either by exhaustion, embolism, or complications is the rule: several recoveries of undoubted cases have, however, been recorded. When speaking of the pathogeny, I mentioned a case in

which malignant endocarditis occurred after an injury, and in which the patient recovered with a damaged aortic valve, and is at the present time in a satisfactory state of health. Another patient, whom I saw with Dr. Hassall of Northwich, with all the signs of infective endocarditis implanted on a diseased aortic valve, recovered.

Treatment.—Many are the drugs that have been recommended in infective endocarditis. Apart from the general treatment with tonics, stimulants, and rest, the same drugs as are given in rheumatic endocarditis—such as the alkalies and salicylates, antipyrin, phenacetin, and so forth—have been recommended, but the results have not been encouraging. Large doses of quinine appear more useful, though the quinine does not prevent the occurrence of the rigors, even in large doses. Fraentzel recommends large doses of quinine with arsenic, and I have for some years given this combination; yet, except in the two cases quoted above, and in a third case in which the symptoms of endocarditis occurred after an attack of gonorrhœa, and in which there was also a peri-urethral abscess, the fatal termination was not averted.

Benzoate of sodium, recommended by Kleber and others, has not given any good results in my hands.

Sulpho-carbolate of soda (half-drachm doses) is recommended by Dr. Sansom, who records one case in which, when death took place at a later period, distinct cicatricial tissue was found at the site of the old ulcerations.

Antistreptococcic serum, administered subcutaneously, has been tried in a number of cases, and with results more encouraging than have been obtained by any other method. Sir R. Douglas-Powell in 1898 reported three successful cases, and among the recorded cases found 25 per cent of recoveries. In 1903 Dr. Cyril Ogle found, from the records of 19 cases, in which an attempt had been made to identify the organisms present in the blood, a higher percentage of recoveries from the use of antistreptococcic serum, viz. 31·5. More recently, Dr. Newton Pitt has reported two cases in which recovery followed the use of the serum, and I have noted recovery in two cases, and a temporary improvement in a third which is still being treated with antistreptococcic serum. Sir Dyce Duckworth has recorded recovery in one case following the administration of the serum per rectum in doses of 10 c.cm. On the other hand, only negative results have been observed by some writers. Dr. Nathan Raw used antistreptococcic serum in five cases without benefit; and Dr. Glynn records no encouraging results from the Liverpool hospitals nor from his own experience in three cases. As important factors contributing to the success of this method there are to be noted, that the serum should be polyvalent, it should be administered early in the disease, subcutaneously, and in doses of from 10 to 20 c.cm.

In a case recorded by Moritz, in which staphylococci were demonstrated in the blood, antistaphylococcic serum was successfully employed. Sir R. Douglas-Powell has tried subcutaneous injection of yeast in five cases,

but without any marked result; and in one case nuclein was used, which caused a temporary fall of the temperature

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CEREBROSPINAL FEVER

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SYNONYMS.—Epidemic cerebrospinal meningitis, malignant purpuric fever.

Cerebrospinal meningitis, in its epidemic form, is a disease of which we in England have had very scanty experience. Yet there are reasons why we should not neglect to consider it; for its historical and geographical interest is great; and a country, hitherto comparatively immune, cannot expect always to escape outbreaks in the future.

This disease was not recognised till the beginning of the nineteenth century; within that century there have been two widespread epidemics of it in Europe, and three in the United States. Professor Hirsch, upon whose exhaustive writings I must largely draw, divides the history of epidemic cerebrospinal meningitis into four periods. The first of these periods ranges from 1805 to 1830. In Europe the outbreaks were then isolated and not very extensive; as at Geneva (1805), at Grenoble and Paris (1814), Metz (1815), in the province of Genoa (1815), at Vesoul (1822), in Westphalia, and possibly at some other places, as for instance, in Sunderland (1830). But in the United States this period was characterised by a widespread epidemic, including the New England states (1814 to 1816), and other more westerly states as far as Kentucky and Ohio (1808). Nor was Canada altogether exempt.

The second period is from 1837 to 1850. France was first attacked: in 1837 the disease began in two separate districts of the south of France—namely, Bayonne and the valley of the Adour on the one hand, Foix and Narbonne on the other—and thence spread through towns of S.W. and S.E. France respectively. In many instances the epidemic was limited to the garrison of a town; and an epidemic at Versailles appeared to be produced by the transference thither of soldiers from an infected spot. Other independent foci appeared in N.E. France, as at Metz (1839 to 1840), and N.W. France, as at Laval (1840), Brest, Caen, and Cherbourg, whence the disease also spread mainly, but not wholly, among garrisons. These outbreaks continued till 1842 and then abated, but from 1846 to 1850 a fresh series appeared, chiefly in garrison towns of N.E. and S.E. France, but also in Orleans and Paris. Throughout this French epidemic the central parts of France were the least affected. Coincidently, and doubtless in connexion with the French epidemic,

there occurred an epidemic in Algiers (1840 to 1847). Southern Italy and Sicily were severely attacked between 1840 and 1845, the disease spreading widely among the villages. In Denmark also and Iceland the disease was widely prevalent between 1845 and 1848. In no other European country was there a severe and extensive pestilence, though minor outbreaks were reported from various places, as from Gibraltar in 1847 (2). In Great Britain certain cases appeared in Irish workhouses in Dublin, Bray, and Belfast (1846), and some at Liverpool. The United States were again the theatre of a widespread epidemic, which manifested itself in the western and southern states, "at places as remote as possible from Transatlantic communication, and hundreds of miles distant from each other" (3). Somewhat later it appeared in Pennsylvania (1848), and at New Orleans (1850).

The third period, 1854 to 1874, exhibited quite a different distribution of the disease in Europe. The countries of South and West Europe (except for a somewhat wide epidemic in South Italy, an outbreak in Portugal and one in Ireland) were spared; Sweden, Germany, and some parts of Russia were the chief sufferers. Beginning at Gothenburg in 1854, and reinforced from other foci in the south of Sweden in the following year, the disease spread through Sweden in a northerly direction. The outbreaks, which proved extremely fatal, appeared in winter or spring time, and gradually extended northwards till in 1858 the latitude of 63° N. was reached. After that year the pestilence gradually declined. The neighbouring countries of Norway and Denmark did not wholly escape. In 1861 to 1862 there were outbreaks in Portugal. Next Germany was widely ravaged. The disease appeared in North Germany, namely, in the eastern districts of Silesia (1863), Posen, Pomerania, East and West Prussia; and also in Brandenburg, Saxony, Hanover, etc. Southern Germany was severely attacked; beginning at Erlangen and Nuremburg (1864), the disease spread over the bulk of Bavaria, and appeared also in Hesse and Baden. The acme of the German epidemic was in 1864 and 1865; after 1866 the outbreaks became limited and scanty. Austria and Hungary largely escaped. Russia suffered at various points, and notably in the Crimea (1867 to 1868). At Dublin and in some other parts of Ireland (1866 and 1867) there was an epidemic which affected both the troops quartered there and the civil population. There were some scattered cases in England, namely, in Rochester and South London, and a small epidemic at Bardney in Lincolnshire. The United States witnessed a third great epidemic. This began in North Carolina and in New York State (1856 to 1857), spread widely during the War of Secession (1861 to 1863), and afterwards covered nearly the whole area of the States, and did not subside till 1874.[1]

[1] Stillé's table (1883) of the annual deaths from this cause in Pennsylvania showed that although the numbers dropped from 246 in 1873 to 82 in 1874, they still remained high, ranging from 56 to 90 per annum. Pepper's continuation of this table shows a sudden rise in 1884 to 124 deaths, then a decrease to 23 in 1891.

Hirsch's fourth period, namely, from 1876 to 1884, which we may fairly carry on to the present time, is one of quiescence. In 1905 there was an extensive epidemic with high mortality in New York. In Great Britain we may mention sundry minor attacks, as at Dublin (1885 to 1888, and again in 1900), Birmingham and its neighbourhood (1876), Galston near Kilmarnock (1884), and certain villages in the eastern counties (1890).

Epidemic cerebrospinal meningitis may be regarded in a twofold light: (1) as an acute specific fever; (2) as a disease which, like many other specific fevers, is characterised by certain definite local lesions.

Morbid Anatomy.—This consists essentially in an acute inflammation of the pia-arachnoid, both of the brain and cord, usually manifesting itself by a purulent effusion into the sub-arachnoid space. In some few cases, indeed, where death has taken place at a very early stage, no effusion may be perceptible to the naked eye, nothing more being evident than mere hyperæmia, or (it may be) cloudiness of the membranes. Even then, however, the microscope may show that they are infiltrated with cells. But most commonly the effusion is visible. This when quite recent may appear serous or simply cloudy, or it may be blood-stained, or again it may be transparent and gelatinous in consistence; but most commonly it is purulent, either yellowish and semi-solid, like butter, or a purulent liquid. Such purulent effusion has, indeed, been found where death took place only five hours after the onset (4). The pus is in the sub-arachnoid space, and thus remains *in situ* after removal of the dura. Upon the brain it is distributed either at the base only or over the hemispheres, or in both places, and also upon the cerebellum. It may occur in streaks and patches along the line of the vessels, or in the recesses of the fissures and sulci, or in a more or less continuous sheet covering the whole brain. Of the cord it affects by preference the posterior aspect, and the dorsal and lumbar regions and cauda equina, rather than the cervical region; but the whole cord may be covered by it and the nerve-roots as well. An effusion, though less frequently purulent, may take place into the ventricles of the brain, resulting from inflammation of the choroid plexus. There is therefore little to distinguish acute meningitis of the epidemic type from other forms of purulent meningitis. The aspect of the meningeal disease differs according to its duration. Thus in the most acute cases the purulent infiltration is visible only under the microscope; in cases of slightly longer duration there is abundant fibrino-purulent exudation; but in chronic cases there is thickening of the meninges, either with or without exudation.

The effusion consists, according to von Ziemssen, of pus cells, granules, fibrin, and mucin. Micrococci have been found in it—to which point we shall return later. Sir J. Burdon-Sanderson says the cells bear a general resemblance to pus cells, but are less uniform in size and character. They may form almost a continuous layer, or may be embedded in a granular amorphous interstitial substance.

Flexner and Barker in the two cases they examined found lympho-

cytes, polymorphonuclear leucocytes, and larger cells of epithelioid type with vesicular nuclei, and some red blood-cells. There was an amorphous intercellular substance staining deeply with logwood; a little fibrin in one case and none in the other.

Councilman and his colleagues found, in the acute cases, polymorphonuclear leucocytes either closely packed together, or embedded in granular coagulum, with very little fibrin; in more advanced cases a larger number of leucocytes, with occasional red blood corpuscles, and a certain amount of fibrin, but not nearly so much as in tuberculous or pneumococcal meningitis, and in addition certain large epithelioid cells, regarded as derived from connective-tissue cells or from the cells which line the lymph-spaces of the normal meninges. In chronic cases the meninges are converted into cicatricial tissue containing only scanty patches of cells, which are now no longer of the epithelioid type, but are chiefly lymphocytes, or plasma-cells. They think that in meningitis due to the meningococcus (*vide* p. 938) the exudation is less fibrinous than in that due to the pneumococcus, and that there is less disease of the blood-vessels.

The subjacent nerve-centres are also involved in the morbid process. This may be recognised to a certain extent from their naked-eye appearance—the surface of the brain being either congested, or, perhaps more commonly, sodden, soft, and pale—but it is more definitely ascertained by microscopic sections. These show that the cell-infiltration spreads, as we might expect, by contiguity into the superficial layers of the brain and cord, and further that it penetrates still more deeply along the sheath of the vessels that dip into the nervous substance. Microscopic abscesses and hæmorrhages may thus arise, and sometimes these are large enough to be visible to the naked eye.[1] Changes in the nerve-roots and their ganglia are also wrought by the spread of the inflammation from the meninges.

There is little to be said about the other organs of the body. The skin may exhibit the remains of eruptions. There may be marked post-mortem lividity, fluidity of blood, and ecchymoses of internal organs, as in other acute specific diseases. The skull-bones and dura are often highly congested. Sometimes there is acute inflammation of the cavities of the nose, or of the ear. The spleen may or may not be enlarged. Bronchitis, bronchopneumonia, and hypostatic congestion of the lungs may be present (the patients often dying from pulmonary embarrassment). Sometimes there is lobar pneumonia or acute pleurisy; sometimes endocarditis or pericarditis. But meningitis is the essential lesion.

Any description of the **symptoms and course** of this disease must be prefaced by the statement that they are liable to much more variation

[1] Strümpell, who has drawn special attention to this process, believes that the inflammation thus set up is by no means limited to the surface of the brain. He also thinks that a large localised abscess may arise after, and in consequence of an attack of epidemic cerebro-spinal meningitis.—*Deutsches Archiv f. klin. Med.* xxx. pp. 523 foll. Councilman considers that such lesions of the nervous tissues are most marked in the particular form of meningitis which is produced by the meningococcus.

than is usual in specific fevers, both in different epidemics and in different cases of the same epidemic. Nevertheless there are certain cardinal symptoms; namely, on the constitutional side—fever of sudden onset, with depression of the vital powers, with or without rash; on the nervous side—pain in the head and neck, retraction of the head, and oftentimes delirium and coma; and out of the commonest symptoms and their most frequent association authors have endeavoured to construct a "*simple type*" of the disease.

In the *simple type* there may be prodroma, such as chills, malaise, headache, vague pains in the back and limbs, but suddenness of onset is a striking feature in most cases. The disease may commence with a rigor, fever, vomiting, or vertigo: but pain in the head, and specially at the occiput, is always an early symptom. This pain is intense, and accompanied or soon followed by stiffness at the back of the neck, or actual retraction of the head. The pain is apt to spread down the spinal column and to radiate into the limbs and abdomen. Along with it there may be tenderness of the skin of the trunk. The eyes are suffused, the pupils (at this stage) are often small, the face pale, and the mind clear; an extreme restlessness is common, a lethargy is less frequent.

In mild cases the disease may stop short here and the symptoms pass off; in severe cases they become worse, the pain increases, the rigidity of the neck spreads down the spine, producing perhaps actual opisthotonus, the mind begins to wander, or downright delirium sets in, which may pass into furious mania. At such a stage, after only a few days' illness, the patient may die, apparently from the mere violence of the nervous symptoms.

But if neither death nor abatement of the disease take place, the delirium is often succeeded by coma. The two conditions may alternate, or the coma may be persistent and eventually deepen into death. But should the coma also clear up, the patient, after a varying interval, and in an extreme condition of emaciation and enfeeblement, enters on a tedious convalescence.

Other common events are—(1) cutaneous eruptions, notably herpes, and petechial spots; (2) affections of the eye and ear, which too often prove irremediable.

The duration of the attack varies greatly—from two or three days to three or four weeks or more. Death may occur, or recovery set in, at different stages, and such recovery may be complete, or may leave the patient with persistent headache, or crippled in limb or special senses.

Numerous other types are described. The most important of these is the "type foudroyante" of French authors, which may also be called the fulminant, siderant, apoplectic, or *malignant type*. The characteristics of this are extreme suddenness of onset, severe collapse, and early coma, which may prove fatal ere diagnostic symptoms have appeared. Cutaneous hæmorrhages, often extensive, are common in this form of the disease. Recovery is a rare event. Such cases are comparable to

the malignant forms of measles and of other specific fevers, in which the patient, overwhelmed by the poison, dies early. They are said to be most common at the commencement of epidemics, and obviously this must render the diagnosis of their true nature more difficult.

The *abortive type* is that in which the patient suffers for a short time and in a limited degree from vertigo, headache, occipital pain and the like, but recovers rapidly without any serious illness. Similarly during cholera epidemics, cases of simple diarrhœa are often prevalent; and during epidemics of scarlet fever or diphtheria cases of sore throat.

The *intermittent type* is a curious variety. In this there appear alternate remissions and exacerbations of the symptoms. Sometimes these appear to have the periodicity of true ague; but according to von Ziemssen the regular use of the thermometer shows that the periodicity is more apparent than real. This peculiar tendency may be observed in any stage of the disease, even in the prodromal period where such exists.

The clinical features of the disease must be considered more in detail; and first, the general features. Acuteness of onset and violence of local symptoms are dominant facts. Yet *the temperature* does not necessarily run high. All authors agree that the temperature is not characteristic, it neither corresponds to the type of any other fever, nor has it a type of its own. Maintained elevation of any high degree is exceptional; 101° to 103° F. appears to be about the average. But, as in other diseases of the nerve-centres, sudden rises may take place, which are either transitory or prolonged into veritable hyperpyrexia. Neither can any rule be laid down about the *pulse-rate*; it is rarely much accelerated, except it be towards the end of a fatal coma; it may vary greatly from time to time. But in character the pulse is compressible and of low pressure, not hard or bounding; in this respect corresponding to the general loss of strength, prostration, and tendency to collapse which from the outset form a striking feature of the disease.[1] There is no constant increase in the *respiration*-rate; the character of the respiration in the early stages may be simply indicative of pain, but in the graver conditions it becomes embarrassed and "suspirious," marked, that is, "by a slow, laboured inspiration followed by a quick expiration and a long pause" (5). When with deepening coma there is a steady rise in the pulse-rate, respiration-rate, and temperature, with blueness and a clammy skin, a fatal pulmonary paralysis is indicated. The *tongue*, except in very severe cases or towards the later stages, when a so-called typhoid condition has appeared, may give no indication that the patient has a grave constitutional disease. The *bowels* are usually confined. There is neither burning heat of *skin* nor profuse sweating. The *conjunctiva* may present a diffuse pink suffusion upon which some authors lay much stress (3); the *face* is usually pale, and till stupor or delirium intervene

[1] I do not find that authors lay much stress on slight irregularity of pulse, such as is common in tuberculous meningitis, though von Ziemssen remarks that irregularity in rhythm is not uncommon.

the expression is not dazed and heavy, but indicative of pain, restlessness, and irritability.

The *urine* is normal, but sometimes contains albumin, and in hæmorrhagic cases blood; glycosuria has been observed rarely (8, 9).

The *blood*, as obtained by venesection, shows, according to Stillé, the characters indicative of inflammation; while from microscopic examination Flexner and Barker conclude that there exists in the early stages of the malady a well-marked leucocytosis, associated with certain other changes, not peculiar to this disease, which may exist in any kind of local inflammation with exudation. Other authors confirm this: thus in thirty-three cases reported by Councilman, there was a leucocytosis (ranging from 9350 to 31,000) in every one. The leucocytosis was due to an increase in the number of polymorphonuclear leucocytes. In Prof. Osler's cases the leucocyte count ranged from 7600 to 47,000. But this leucocytosis has not the prognostic significance that it has in pneumonia: nor does it aid in the diagnosis of epidemic from other forms of meningitis.

The *nervous symptoms* must evidently be similar to those which occur in other forms of meningitis, but their acuteness and severity are greater.

The *headache* is not a mere dull aching, but an intense and often an intolerable pain. Without definite localisation at first, it soon concentrates itself upon the occiput and back of the neck. *Pain*, too, may affect the spinal column, and may radiate thence into the limbs and round the trunk, and into the abdomen particularly; so that in some cases abdominal pain becomes quite a leading symptom. The pain is aggravated by all movements.

Cutaneous hyperalgesia is common. This probably originates, like the pain, in irritation of the sensory nerve-roots. Numbness and anæsthesia may follow as the nervous irritation gives place to paralysis.

The pain is accompanied or soon followed by another symptom, so common as to be almost pathognomonic, namely, *retraction of the head*. The head is thrown backwards (in extreme cases so far that it appears to lie between the scapulæ), the patient generally lying on his side with the legs drawn up. Sir J. Burdon-Sanderson thinks this pose of the head is assumed in order to mitigate the pain in the muscles of the nucha; but most authors regard it as due to a tonic muscular spasm. Sometimes the extensor muscles of the whole back are implicated so that there is actual opisthotonus. The limbs also may become rigid, or the face may be drawn into a risus sardonicus, or in bad cases there may be trismus. All these muscular spasms are more continuous than those of tetanus, not presenting such perfect alternations of paroxysm and remission as does that disease.

The phenomenon known as *Kernig's sign* may be mentioned here. This is a spasm of the hamstring muscles induced by the attempt to extend the knee-joint, while the hip-joint is semi-flexed. If the patient can sit on a chair the spasm is produced by simply straightening the knee. If he is lying on his back or side, the hip-joint must first be semi-

flexed, then the attempt to straighten the knee produces the same effect. It is generally evident that this manipulation hurts the patient, and probably Netter's explanation is correct that the spasm is produced by the pain which traction on the inflamed nerve-roots causes. In cases of sciatica pain can be produced in a similar way. Kernig's sign is common to all kinds of spinal meningitis.

Vomiting is another early symptom; it is of more common occurrence, more severe and intractable than in most other fevers. It may occur independently of food, without furring of the tongue or other signs of gastric disturbance, and is therefore to be ascribed to the irritation of the nervous system. Vomiting in the later stages of the disease, especially when associated with coma and convulsions, is indicative of distension of the ventricles by effusion, and is of bad import (7).

There may be distressing *vertigo*, particularly when the patient lifts his head from the pillow; this may be sufficiently accounted for by the derangement of the cerebral centres, but it must be remembered, too, that sometimes the auditory apparatus is specially involved.

Twitchings of the limbs are very common, general *convulsions* may occur, but (except in children) are less frequent than we might expect, considering the amount of cortical irritation. Prolonged convulsions are a bad sign, particularly when they occur late in the disease.

Paralysis of the ocular nerves, causing squint (possibly in some cases due to muscular spasm), ptosis, dilatations and inequalities of the pupils, are as common as in other forms of meningitis. *Nystagmus* is sometimes seen. Facial paralysis may also occur. Paralyses of the limbs do not appear to be common; still they may occur, and particularly in the later stages: they may be of very various types (hemiplegic, paraplegic, monoplegic), as is evident from the wide distribution of the lesion; and may be transitory or permanent, according to the degree of damage to the nerve-roots and centres.

The *tendon-reactions*, according to Strümpell, may vary. Thus, in thirty-two cases examined by him in Leipzig in 1879, the knee-jerks were absent in five; in three they disappeared, to reappear during convalescence, which change was probably due to varying pressure on the nerve-roots; sometimes they were lively, sometimes much increased.

Optic neuritis was found by Randolph of Lonaconing, Maryland, six times in forty cases examined ophthalmoscopically; but in thirty-six cases reported upon by Dr. Travers Smith in Dublin, well-marked optic neuritis was not found once.

The mental condition we have already noticed. Extreme restlessness is often a characteristic of the early days of the disease. *Delirium* very commonly supervenes, whether it be a mere wandering at night, or a kind of rambling stupor from which the patient can be aroused by sharply speaking, or an active and often violent delirium. The access of *coma* is always a grave sign, though recovery from it is by no means impossible; the more deep and persistent the coma the worse the prognosis. It must not be supposed that these mental states always

succeed each other in regular order; delirium may occur at the outset, and the worst type of case, the "foudroyante," is marked by early coma.

There are symptoms which cannot be wholly referred to the disease of the nervous centres, and of these the most striking are the *rashes.* These are by no means constant. In some epidemics there has been no rash; in others very various rashes have been described, as for instance erythema, urticaria, rose-spots like those of typhoid, measly cruptions, vesicular and bullous eruptions. But the most common are herpetic and hæmorrhagic rashes.

Herpes of the lips and face is so frequent that it has been called characteristic of the disease.[1] Tourdes observed it in two-thirds of his cases. Von Ziemssen says that in no other disease has he observed facial herpes to spread so widely. It commonly occurs within the first five days of the illness, but sometimes later than this; and, indeed, there may be several crops of herpes coming out at various dates. It has no prognostic significance. Eruptions of herpes zoster may come out on the limbs and trunk, and are often symmetrical; but these, according to Klemperer, stand on a different footing to herpes labialis; the vesicles of the latter containing micrococci and pointing to the inflammatory nature of cerebrospinal meningitis, whereas zoster may be correlated with the nervous lesion. Petechiæ were so common and so abundant in the early American epidemics that the name "spotted fever" was applied to the disease—a name peculiarly unfortunate: first, because of the confusion thereby created between epidemic meningitis and exanthematic typhus; and, secondly, because in many other epidemics petechiæ have not been seen at all. This rash, like herpes, may appear early, and has little relation to the gravity of the disease.

Cutaneous hæmorrhages other than mere petechiæ are a more serious matter, as they generally indicate a severe form of the disease. In the Dublin epidemic of 1866-67 such hæmorrhagic rashes were particularly common, so that the name "malignant purpuric fever" was then propounded. Dr. Samuel Gordon, describing the condition of the skin in this epidemic, notes that there may be—(1) a coldness or blueness of the extremities or whole body like that of cholera; (2) bruises and ecchymoses like those of typhus or scurvy; (3) a hæmorrhagic eruption coming out all over the body, but chiefly in the lower limbs, dark in colour, being brown, purple, or black as ink; some spots small and round, others larger and irregular, others like large spots of very black purpura, but more mottled and more irregular in colour and shape, others raised above the level of the skin. These may be gradually absorbed, or may in some cases become gangrenous. Prof. Osler noticed in three cases a peculiar rash in the neighbourhood of the joints, especially on the extensor surface of the knees and elbows, and about the ankles, consisting of a diffuse but intense livid erythema, on which developed vesicles filled with

[1] Yet Stillé says of the Massachusetts epidemic:—"Herpes labialis was noticed in a few instances . . . it is certainly much less common as a symptom of epidemic meningitis than either the roseolous or petechial spots" (3).

blood; these vesicles subsequently dried up, leaving little nodules which persisted for a week or ten days. Hæmorrhages from the mucous surfaces, for example, of the nose, stomach, bowels, kidneys, may also take place.

There are other important possibilities, which are perhaps best reckoned as **complications and sequels**. Foremost amongst these are affections of the special sense organs.

The eye may be attacked, even in the early stages of the disease, by severe conjunctivitis, or by iritis or keratitis leading to corneal opacities. Still more to be dreaded is inflammation of the deeper parts, such as a purulent infiltration of the choroid, leading to detachment of the retina, or (still worse) to inflammation and disorganisation of the whole eyeball. It is possible that this deep-seated inflammation is propagated from the meninges along the sheath of the optic nerve to the structures at the back of the eyeball. Other ophthalmic complications are optic atrophy, secondary to optic neuritis; thrombosis of the retinal veins; amaurosis.

Disease of the *auditory apparatus* is even more frequent than that of the eye. The onset of deafness may be difficult to time in the presence of a severe constitutional disease, particularly when there is delirium or stupor. But in some cases, at any rate, it is an early symptom. Deafness may be due either to purulent otitis media, or to disease of the labyrinth (15). In the latter case it is probable that the meningeal inflammation spreads along the auditory nerve to the cochlea and semicircular canals. If these parts are destroyed total and hopeless deafness must result; and in little children this means deaf-mutism.[1] With this is sometimes associated a staggering gait.[2]

An acute coryza or rhinitis sometimes occurs, the main importance of which is that the meningococci (presently to be mentioned) have been found in the nasal secretion. Of less importance are *anosmia* and loss of taste, which have also been described.

Chronic hydrocephalus is a very serious sequel. This has been particularly studied by von Ziemssen (7). It would appear that in cases which survive the acute stages of the disease the meningeal exudation gradually degenerates, and is absorbed; but the pia-arachnoid becomes thickened and shrunken, and the ependyma ventriculorum hypertrophies. The ventricular effusion, probably in consequence of these cicatricial changes, either remains unabsorbed or increases in amount, albeit now less purulent and more passive in character; while the cerebral substance

[1] How frequent these aural complications may be is shown by the observations of Moos, who found that out of 64 convalescents from epidemic cerebrospinal meningitis, 38 were deaf-mutes; 20, absolutely deaf; 5, partially deaf; 1, not at all deaf; and 32 had a staggering gait. And von Ziemssen found that, in an institution for deaf-mutes, containing 42 children, every one had become deaf-mute after cerebrospinal fever, while in another of 32 inmates the number due to this cause was 22.

[2] Voltolini's disease, the symptoms of which are deafness, deaf-mutism, and staggering gait, coming on after a short feverish attack, perhaps accompanied with severe cerebral symptoms, which Voltolini ascribes to primary inflammation of the labyrinth, is thought by many physicians to be a meningitis spreading to the ear.

becomes pallid and atrophied from pressure. The symptoms of such hydrocephalus show themselves during the period of convalescence, a distinct interval having elapsed since the acute stage of the meningitis; they consist of headache and pains, vomiting, coma, convulsions. Sometimes they have a paroxysmal character, and may thus last for weeks. The onset of such symptoms at this late stage of the disease must give rise to serious alarm, for recovery from hydrocephalus, though it may take place, is very rare.

Joint disease is not unfrequent; it is mentioned both by the older writers and by several recent authors. Sometimes the joints are painful, red, and swollen, as in gout or acute rheumatism; sometimes there is a simple serous effusion, sometimes they contain pus. This last fact seems to point to infection as the cause of the joint disease, rather than to a perverted trophic influence of the nerve-centres. The appearance of joint affections has in some instances coincided with amelioration of the meningeal symptoms. Non-purulent arthritis has been treated successfully by salicylates.

Pulmonary congestion and collapse are frequent, as is natural in the course of an exhausting acute disease; bronchopneumonia may occur, and sometimes acute lobar pneumonia. It will be remembered that conversely acute pneumonia may be complicated by meningitis; this occurrence, rare on the whole, is said to be more frequent after an epidemic of meningitis than at other times (16).

Other complications, apparently of a *pyæmic* nature, may be mentioned, such as infective endocarditis, pericarditis, pleurisy, peritonitis, parotitis with abscess, and diffuse abscesses in the connective tissues of the limbs and trunk. Sometimes, instead of the usual constipation there is an enteritis, which causes a dysenteric *diarrhœa.*

Lastly, a rapid and great *emaciation* accompanies the disease, which may take long to amend.

As to **treatment,** it must be admitted at once that we have no specific to arrest the morbid process. In the earlier epidemics free blood-letting was employed, not with much success; but local depletion by leeches or cups, or blisters to the temples, nucha, or spine have been much used. Such remedies are suitable only for the early stages of the disease, when they are said to relieve symptoms, and possibly to modify the local inflammation of the meninges. Cold in the shape of ice-bags is recommended for the same purpose. Mercurial purgatives have been freely given, and mercury has been used so as to produce its constitutional effect. One author writes:—"The jugular vein was opened, and blood drawn in a full stream as long as the boy's strength would permit. This was followed up by relays of leeches to the temples and mastoid processes. The mercurial plan was at the same time most energetically pursued, and blisters with mercurial dressings were applied to the head and along the spine. Yet all was of no avail, my patient died in convulsions on the fourth day." All such heroic measures in the way of bleeding, purgation, emetics, mercurialisation, and the like, are

contra-indicated by the tendency to depression and collapse which may exist from the very outset. Such tendency, when present, must be met by alcohol, used sparingly in ordinary cases, liberally in those which are of the malignant type. The diet must necessarily be light at first, while vomiting and other acute symptoms prevail, but it may be increased earlier than in most fevers, as there is seldom any gastric or intestinal lesion, and severe emaciation is common. The importance of carefully feeding comatose patients, by the rectum or by the nasal tube if necessary, need hardly be insisted upon. There is an almost universal testimony in favour of one drug, namely, opium or morphine. Sir J. Burdon-Sanderson says that its advantages in calming restlessness and relieving pain after the initial symptoms have subsided seem unequivocal (in doses of $\frac{1}{8}$ to $\frac{1}{4}$ grain of opium by the mouth, or better as morphine hypodermically). Von Ziemssen says, "Morphia may be regarded as one of the most indispensable remedies in the treatment of epidemic meningitis." Stillé, going further, gave one grain of opium every hour in severe cases, or one grain in moderately severe cases every two hours, under the conviction that it is not merely a palliative, but also influences favourably the whole condition of the patient, and that the opium treatment is most useful when it is begun early in the attack.

Warm baths given three times a day, or oftener in the case of children, are highly spoken of by Aufrecht, Netter, and others. In conjunction with such bathing Netter prescribes salicylates for the antipyretic and analgesic effects.

In the later stages of the disease, for such symptoms as may depend upon meningeal thickenings and deposits, iodide of potassium is the best accredited remedy, with tonics to restore the exhausted strength. But for secondary hydrocephalus, von Ziemssen says, little can be done. Local paralyses must be treated by massage and electricity. For the severe disorganisations of eye and ear nothing can be done.

Prognosis.—The course of the disease, as already mentioned, is very variable, but the outlook is always serious. In the fulminant or malignant cases, where the patient is stricken down suddenly and rapidly passes into coma, recovery is very rare. In mild cases, at the end of the first few days, after the irritative stage of headache, vomiting, and perhaps even delirium, the disease may take a favourable turn and convalescence begin. Such convalescence is sometimes rapid, but more often slow. "The disease is distinguished by the slowness of its cure and the rapidity of its fatal issue," says Tourdes. But death may occur during the stage of delirium, or still more commonly during coma, in any case comparatively early: Simon and Sanderson say, "generally from the fifth to eighth day"; Hirsch says, "commonly within the first eight days, and as a rule between the second and fourth day." Nor are the later stages free from danger, looking to the risk of hydrocephalus and to the extreme exhaustion and emaciation.

The prognosis is influenced:—

1. By the character of the epidemic; Hirsch's tables of forty-one

epidemics give all grades of mortality from 20 to 75 per cent (17); and by the duration of the epidemic, for rapidly fatal cases are most frequent at the commencement of an outbreak, mild cases towards its close.

2. In the individual case by the following circumstances :—

Absence of prodroma, sudden and severe onset, early appearance of coma, depth and prolongation of coma, wideness in the distribution of the local nervous symptoms (showing brain and cord to be alike involved), trismus, complications involving other organs—especially the lungs, the reappearance of grave cerebral symptoms (vomiting, convulsions, coma) in the stage of convalescence; all these things are unfavourable.

As to age, Hirsch says that children and people over forty run greater risk than those of middle age. Concerning a Dublin epidemic Grimshaw says that of the children admitted to Cork Street Hospital many recovered, while the recruits admitted to Steevens' Hospital mostly died.

The **diagnosis** should in general be aided by two considerations :—

1. The knowledge that an epidemic prevails.
2. The appearance of meningeal symptoms early in the illness.

There are not many epidemic diseases with which confusion is likely. Typhus may resemble it in the rash, the prostration, and the coma; and true typhus may be complicated by meningitis; but the attack of epidemic meningitis is more sudden, there is no regular upward march and maintenance of temperature, the initial headache is more severe and persistent, and the meningeal symptoms come on early. Influenza presents similarities in the sudden onset with fever, headache, and pains in the back and limbs, and in the prostration to which it gives rise. In coincident epidemics of the two diseases, it might indeed be difficult to distinguish severe influenza from mild meningitis; but in general the shorter course, the less serious character of the nervous symptoms, and the absence of retraction of the head, and of positive signs of organic nervous disease (such as squint, etc.), would point to influenza rather than to meningitis. Should an epidemic of meningitis begin with fulminant cases, which prove fatal before nervous symptoms set in, it may be impossible to recognise their true nature at the time. The opposite difficulty may occur when an epidemic is characterised by many mild or abortive cases; in that event minor complaints, such as rheumatism of the neck, migraine, hysteria with opisthotonus, may be taken for meningitis, and particularly febrile diseases in children beginning with convulsions, vomiting, nervous irritability, and perhaps with retraction of the head.

Tuberculous meningitis (in children, at any rate) has generally a more gradual onset, a less violent headache, and a more regular course than the epidemic disease.

In acute meningitis of the ordinary type diagnosis is aided by the presence of a recognised cause, for example, suppurative disease of ear or nose, disease of bone, injury, pyæmia, or other acute illness; moreover, spinal symptoms are less commonly present.

Lumbar puncture is now considered to be a valuable aid in diagnosis. It may enable us to say whether meningitis exists, and what form of it is present. The needle is usually introduced into the subarachnoid space between the fourth and fifth lumbar vertebræ, or between the fifth lumbar vertebra and the sacrum. The first of these two spaces is on the horizontal line between the summits of the iliac crests. The lumbar spines must be made as prominent as possible by flexing the back, and the needle introduced either in the middle line directly, or at a point about $\frac{3}{8}$ of an inch to the right of it, with an inclination towards the middle. This latter course is recommended in adults to avoid the interspinous ligaments. To reach the subarachnoid space in this way the needle should penetrate, according to Councilman, 3-4 mm. (about $1\frac{1}{2}$ inches) in children, and 8-9 cm. ($3\frac{1}{4}$-$3\frac{1}{2}$ inches) in adults. The cerebrospinal fluid should be collected in a sterilised test-tube. Normally it is clear and does not deposit on standing. But in most cases of meningitis it is either purulent or turbid or deposits on standing. The deposit, separated by sedimentation or centrifugalisation, is examined for cells and for micro-organisms. If micro-organisms can be found and identified, great light may be thereby thrown on the exact nature of the meningitis.

Isolated cases of cerebrospinal meningitis occur without obvious causation, and the recognition of them before death may be very difficult. Whether such sporadic meningitis is essentially the same as the epidemic or no, we can hardly say till we have attained more certain knowledge concerning the etiology of the two varieties. The rash which is so striking a feature of many epidemics, and which seems to assimilate them to acute fevers in general, is absent in most sporadic cases, but not invariably. It is said that sporadic cases crop up particularly in places which have suffered from the epidemic disease (19); if this be so, it points to the identity of the two varieties.

Etiology.—Cold contributes to the outbreak, but cannot be the sole cause. Most epidemics have begun in winter or spring, and further the attack seems in individual cases sometimes to be determined by exposure to cold. But, on the other hand, in many of the severest winters there have been no epidemics, and recrudescences of epidemics have begun during spells of mild weather. Neither is the disease known in Arctic climates, but only in the temperate and subtropical zones. Hirsch gives its limits in W. hemisphere from 45° N. (Montreal) to 30° N. (Mobile); in E. hemisphere from 63° N. (Sweden and Russia) to 30° N. (Jerusalem, Persia, Algiers).

It is independent of malaria, and of local peculiarities of soil and situation: this is shown by its very wide distribution over different countries, altitudes, and soils.

It has no special predilections for race or sex; as to age, it selects principally children and adults in the prime of life. As to conditions of life, it may be that privation, overcrowding, bad sanitation,—in short, the circumstances of the very poor,—favour its outbreak, but they have never been shown to form an essential cause thereof. It has been seen

alike in town and country. One fact, however, is most prominent, namely, that soldiers are especially obnoxious to it, and particularly, as it would appear, during garrison life. Recruits, too, suffer more than seasoned troops. Particular battalions or regiments, or again particular barracks, have sometimes been picked out by the disease. The counterpart to this has been seen in civil life, when a particular workhouse or school has been selected by it.

The manner of its appearance and spread is peculiar. It spreads from no one centre of origin or of activity either by contiguity or on special lines, whether lines of traffic or other mode of distribution;[1] but it breaks out at diverse and apparently disconnected foci, in separate towns, villages, or tenements; and it spreads in a similar discontinuous way. Netter says that the French epidemic of 1836-1848 "advanced not as an army corps with serried ranks, but rather irregularly and without any apparent order, like squads of skirmishers." In point of time, an epidemic of meningitis does not steadily mount to a maximum and then decline, but proceeds by fits and starts, crops of fresh cases appearing at irregular intervals.

Its ordinary methods of propagation are not known. It has not been traced to food or water-supply. Direct propagation from one patient to another is certainly not the rule, albeit there are a few instances of this. There may be a certain infection of locality, for, as already said, it may hang about places where it has once appeared; and it has been transferred from place to place by human beings, and apparently by clothes.[2]

I find but few statements bearing on the question of immunity, as to whether one attack protects against another; there are, however, one or two cases reported in which the same individual suffered from this disease more than once.

Although epidemics of meningitis have coincided with or followed epidemics of other specific fevers, such as typhus, cholera, and others, it has no constant relation with any one of them, and its history and clinical features are sufficient to stamp it as specifically different from them, and probably dependent on a virus of its own.

Can we go further, and say what this virus is?

Cases of meningitis may be roughly divided into two groups: (1) Secondary meningitis, where there exists in the body some obvious focus of infection; (2) Primary meningitis, where no such focus is discoverable. Secondary meningitis may be due to micro-organisms of very various kinds, such as the tubercle bacillus, the pneumococcus, staphylococci and streptococci, the bacillus of influenza, of typhoid, and others. But primary meningitis, it would seem, is always due to one or other of two organisms, either (*a*) the diplococcus pneumoniæ of Fränkel, shortly called the pneumococcus, or (*b*) the diplococcus intracellularis meningitidis of

[1] There are a few exceptions to these statements, for example, the transference of the disease when troops have been moved from place to place, and the Swedish epidemic which spread steadily in one direction (*vide* p. 924).

[2] See Kohlmann's cases, as quoted by Netter.

Weichselbaum, which may be shortly called the meningococcus. The characters of the pneumococcus are too well known to need recapitulation; those of the meningococcus are much as follows.[1] It occurs in pairs or tetrads, very rarely in chains, the individuals of the pairs being rounded externally, but flattened at their opposed sides; it is not enclosed in a capsule; it is found mostly within the cells of the exudation; it does not stain with Gram's method; it grows badly in many culture media, serum-agar or Löffler's mixture being the best media for it; its virulence when injected into animals is not great, white mice are most susceptible to it; it is not tenacious of life outside the body, since it requires a special temperature (25° and 42° C. are the minimum and maximum compatible with life), and it is easily killed by drying. It is not certainly known to exist outside the human body, nor in normal human secretions (the nasal secretion being a possible exception).

Primary meningitis again falls into two clinical types: (1) the sporadic form, cases of which are found in all countries and at all times; (2) the rarer epidemic form. There is little difficulty in admitting that the sporadic cases may be caused sometimes by the pneumococcus, sometimes by the meningococcus. But, as regards the epidemic form, we must allow the force of Professor Osler's remark, that it seems very improbable that such a remarkable specific affection as this should be caused by two different organisms. If, however, only one be admitted, then the meningococcus must be this one, for its presence has been conclusively established in certain recent epidemics by skilled bacteriologists.

Nevertheless the question is not, perhaps, absolutely decided. In the first edition of this work we gave a summary of the earlier bacteriological investigations into epidemic meningitis wherein a certain *primâ facie* case was made out for the view that the pneumococcus is the organism responsible for it. (This summary we give here in a footnote.)[2] Doubt-

[1] These are taken from Weichselbaum's article in Kolle and Wassermann's *Handbuch der pathogenen Mikroorganismen*. Berlin, 1903.

[2] (*a*) Jaffé, studying an epidemic in Hamburg (1879), could find no micro-organisms in the meningeal lymph.

(*b*) Giuffre, in a Sicilian epidemic of 1882, found oval cocci in the meningeal lymph, not in the blood nor in the spleen. Attempts at cultivation and inoculation failed (30).

(*c*) Ughetti, in Sicily, 1883, found micrococci in the meningeal exudation and the blood: inoculation failed (31).

(*d*) Marchiafava and Celli found diplococci both free and within the cells in the meningeal exudation; cultures were negative (32).

(*e*) Netter states that, in an outbreak at Blois and Orleans in 1886, the micrococcus lanceolatus was found in the spinal and cerebral exudation by Widal.

(*f*) Friis, at Copenhagen, 1886, isolated and cultivated a bacterium in the shape of short thick rods, not unlike an oval coccus; inoculations failed.

(*g*) Four cases from an epidemic at Turin, 1888, were investigated by Foa and Bordone-Uffreduzzi; they found a micrococcus which they identified with Fränkel's, cultivated it and experimented with it; injections into the cranial cavity produced acute general sepsis with cerebral and spinal meningitis. Two of their four cases had pneumonia.

(*h*) At an epidemic near Padua in 1890, Bonome obtained from the meningeal exudation a micrococcus resembling in some degree the pneumococcus, but differing from it in the peculiar tangled growth which it forms on agar, in its inability to grow in blood-serum, and in some of its effects on animals. This he believes to be the specific micrococcus of epidemic cerebrospinal meningitis. There was no pneumonia in his cases.

less some of these observations were imperfect, since the rival organism was not known till Weichselbaum's publication in 1887 and 1888. Still, they cannot all be dismissed in this way, for Weichselbaum himself, reviewing the whole subject in 1903, concludes that we cannot affirm with certainty that all such epidemics are due to the meningococcus, but that we must allow some of them to be due to the pneumococcus.

Whether this duality of causation really exists, and if so, whether epidemics caused by the one agent differ clinically from those caused by the other; or even whether (as suggested by Netter) the two kinds of micro-organism are less distinct than is commonly supposed, are questions still deserving consideration.

APPENDIX

It may be of interest to English readers if I refer briefly to the outbreaks of this disease which have taken place in the United Kingdom. Many of these (though the Irish epidemic of 1866 and 1867 constitutes a notable exception) can scarcely be called epidemics, and some indeed are merely groups of two or more cases occurring at the same time and place. Yet their essential identity with the epidemic meningitis of the Continent and America is, in some instances, hardly to be doubted, and in others is very probable.

1807.—In 1807, at Blackaton, a small village on Dartmoor, a peculiar group of cases was observed by Gervis, the nature of which, in the absence of a post-mortem, remains somewhat uncertain, but they may possibly have been instances of this disease. There were five cases, four of them in one family, and four of the five died very rapidly. Headache, vomiting, collapse, slight convulsive movements, sore throat, and a hæmorrhagic rash are mentioned as symptoms, but no retraction of the head.

1830.—In the autumn of 1830, at Sunderland, several cases occurred, in one of which meningitis was found post-mortem (41).

1846.—The first Irish outbreak occurred in the first half of 1846; there were cases in the workhouses of Belfast, Bray, and Dublin, mostly in boys under twelve years old; and two fatal cases in the Hardwick Hospital, Dublin (42).

During the same year Whittle records cases in Liverpool, some of which he distinctly ranks with epidemic meningitis as seen in Ireland and on the

(*i*) Mirto in 1891 (37), as quoted by Flexner and Barker, discovered in some epidemic cases the typical micrococcus lanceolatus.

(*j*) Herwerden (1893) (38) gives the case of a woman who died of this disease in an advanced stage of pregnancy. Cæsarean section was performed, the child lived five and a half days, and then died of meningitis complicated with pleurisy. In the meningeal exudations both of mother and child, and in the blood, the liver, and the kidneys of the child, pneumococci were found. The virulence of these appeared at first to be slight, but it was increased by submitting them to the action of hydrogen and oxygen, so that injection of them into rabbits produced meningitis.

(*k*) Leichtenstern (39), writing in 1893 of epidemics in Cologne and the neighbourhood in 1885-1892, says that he found the pneumococcus in cases where there was pneumonia, but not in other cases. The special micro-organism he considers to be not the pneumococcus itself, but a variety or "specific derivative" of it.

(*l*) Lastly, Flexner and Barker, in an epidemic at Lonaconing, Maryland (1893), found the diplococcus lanceolatus in the meningeal exudation, both free and enclosed in cells; but their cultures and inoculation experiments did not succeed well.

Continent. Of nine such cases three were fatal. Some, on the other hand, were of a milder type.

In 1846, also, a case was seen at Haslar Hospital (44).

1846-1850.—It would seem from the statements of M'Dowell that from the time of the first Dublin outbreak mild cases presenting symptoms of meningitis continued to appear in Dublin till 1850 at least.

Three cases of somewhat doubtful nature are mentioned at Rochester in 1850 (44).

1864-1868.—At Rochester, also, in 1864 and 1865, some four or five cases occurred, one of which was examined post-mortem (46).

During 1865 it appears that there were further cases in Dublin (47); while the succeeding years (1866 and 1867) saw the second Irish epidemic, the most severe manifestation of the disease which has yet appeared in these islands (48). This epidemic raged principally in Dublin, but also affected other parts of Ireland, attacking both military and civil population. It was marked by great fatality, and by the prevalence of hæmorrhagic rashes, so that the name of "Black Death" was at one time proposed for it, and also that of "Malignant Purpuric Fever."

In England about the same time there were some isolated cases: two in London which were rapidly fatal (49), and one at Devizes (50) (May and June 1867). At Bardney, a Lincolnshire village, there was a small epidemic—over nineteen cases, with one death (51). Somewhat later, namely, March 1868, we read of four cases within three weeks at Shorncliffe Camp (52). In 1867, too, there was a fatal case with petechial rash at Stafford, where there formerly had been two similar cases, namely, in 1865 and 1859 respectively (53).

1876-1878.—The Irish epidemic of 1866 and 1867, with the minor outbreaks which we have just mentioned in England, evidently corresponds to the great wave which had just passed over the Continent.

The next notice of the disease is in 1876, in the Midlands. Two cases occurred among the militia at Oxford (54), and an epidemic in and round Birmingham; fourteen cases were admitted to the Queen's Hospital in nine months, and there were others in the neighbourhood (55).

In the winter of 1877-1878 a good many cases were seen at Dundee, several of which had a roseolar rash, or a hæmorrhagic rash like typhus. There seems to have been evidence that the disease was contagious. One case died with rupture of the spleen (56). At Dublin, in the commencement of 1878, there were three fatal cases within two months (57).

1884-1886.—In the spring of 1884 two cases occurred at the Seaman's Hospital, Greenwich (58), and two at the London Hospital (59); but as three of these patients were sailors, the local character of the outbreak cannot be insisted upon. In Dublin, again, during 1885 and 1886 a somewhat serious outbreak took place, largely in the suburban districts, and amongst comparatively well-to-do people (60). There were fifty-two deaths during 1885. Rapidly fatal cases with purpuric spots were not wanting (61).

In 1884 a small but very fatal outbreak took place at Galston near Kilmarnock. Out of seven cases five were fatal, some with extreme rapidity. Personal intercourse was traced between the various patients, so that contagion seemed probable (62).

At Aberdeen, in 1885, Ogston examined the body of a child which died of acute cerebral meningitis; this he referred to disease of the nasal bones, but he

notes that another child of the family died of meningitis, and that the father had symptoms of the same disease.

Similarly, near Faversham in 1886 two deaths occurred in one family from meningitis (64).

1890.—In July, August, and September 1890 (65), there was an outbreak in five neighbouring villages on the border of Norfolk and Suffolk (Oakley, Broome, Scole, Kenton, Bressingham); the symptoms appear to have been typical; there were twenty cases and two deaths; one post-mortem was made, in which evidence of meningitis was found. No cause could be assigned for the disease. In a village thirty miles away, Great Horkesly, near Colchester, there was another case. Near Maldon, in Essex, some obscure and rapidly fatal cases of fever had been seen that same autumn. In certain Lincolnshire villages scattered cases possibly of a similar nature occurred; thus at Willingham, near Gainsborough, a gipsy boy died apparently from pneumonia and meningitis; at Holbeach, near Spalding, a woman died with symptoms of meningitis; and a severe though non-fatal case occurred at Gedney Hill, about ten miles from Holbeach. Two cases are said to have occurred in the preceding year near Oundle, in a village distant about twenty miles from Gedney Hill.

In March, April, May, and June 1890 four cases of idiopathic cerebrospinal meningitis were examined post-mortem at St. Bartholomew's Hospital (66).

In 1900 there was another epidemic in Dublin (67).

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INFLUENZA

By J. F. GOODHART, M.D., F.R.C.P.

IN attempting the description of a disease we are often in doubt how best to set about the task. Influenza offers no exception to this rule, but happily, so to speak, it has over-reached itself, and by the very width of its range of action over the human body has simplified matters in a way that may not at first be apparent. Clearly the only possible presentation of a disease so multiform in its character as influenza, is to describe it first of all, in as full a manner as space permits, on its clinical aspect, and thereafter discuss its pathology and treatment.

It is not well to pay too much attention to the disease as it has appeared in other countries. After all it is the disease as it appears here in England which concerns us; and it is too often forgotten that, although the whole world is kin, yet there are racial and climatic influences that must make some difference in the picture of disease as it has occurred here or there,—a difference which may well come in to throw light upon some of the obscure points in the natural history of a malady, but which is of less importance from the practical standpoint

of its management as we have to deal with it amongst ourselves. As a matter of fact, however, the disease has departed little if at all from certain broad characters, whatever the affected area, and it would appear that it has spread over most of the habitable globe.

Description.—To present the disease at all adequately it is necessary to describe groups of cases. Peacock, in the epidemic of 1848, described a simple catarrhal fever, fever with pulmonary complications, and fever with derangement of the abdominal viscera. But, as if to emphasise its extreme versatility of form, there may be fever without any catarrhal symptoms, and there may even be influenza without fever. Others have described catarrhal, respiratory, nervous, and gastric varieties. In actual experience all groups must necessarily blend somewhat, nevertheless each is sufficiently distinct to demand separate mention.

Description of Common Influenza.—All cases present, more or less, certain features in common; it will be convenient, therefore, to describe first of all what we may call common influenza. A healthy person is suddenly, for many one may say without exaggeration instantaneously, attacked with violent aching of the head and eyeballs; with a pain in the back, perhaps so severe as to resemble the onset of variola; with racking in the bones that could hardly be worse if they were being broken; with a general distressful soreness; sharp fever without any corresponding acceleration of the pulse, and a hard, dry cough, sometimes with coryza as from a bad cold. Often enough there is some little delirium during the first day or two, and not a few cases have even been ushered in by an acute maniacal delirium. The tongue is thickly coated with a white creamy fur, it is flabby, indented by the teeth, and tremulous. The breath has often a peculiarly offensive odour, and the patient suffers from a sudden prostration, both mental and physical, altogether out of proportion to the duration or apparent severity of his illness. The spleen has been found enlarged in some cases. The fever lasts, perhaps, three, four, or five days and then subsides, leaving the patient weak and much depressed, and with a feeling of having undergone a serious illness in a short space of time. In a case within my own knowledge a man lost twelve pounds of body-weight in one week. To add to the discomfort, after a day or two chills are apt to recur, usually down the back. These are followed by profuse sweats, which may be repeated again and again, and perhaps only slowly disappear some time after the more essential symptoms have entirely passed away.

The first case of influenza that I recognised occurred on December 24, 1889. The disease had not then declared itself in epidemic form in England. But, as other observers have stated, cases had occurred at any rate in the two or three weeks previously. A strong, healthy man went to Manchester to play a football match. He went with a bad cold upon him, and there he became so much worse that he returned home again, by which time he was so exceedingly ill that his brother, a medical man, became much alarmed. He was delirious, prostrate, restless, with a temperature of 102° F., a very distressing dry cough, a

generally tremulous condition of the muscles, and a thickly furred tongue. His lungs gave no evidence of pneumonia, but the air entered badly, and plenty of sibilant rhonchi and rales indicated that the bases were engorged—"congested," as I should prefer to say. These various symptoms, combined with a little diarrhœa, gave the case the appearance of typhoid fever, but the temperature, falling almost at once to normal, led to a correct diagnosis, and he rapidly convalesced.

Of the simple catarrhal form, with its prostration and pulmonary congestion, this is an ordinary case of moderate severity; but there are cases in which the poison is apparently much more virulent, and where in consequence the disease assumes still more of the characters of typhoid fever. A striking example of this occurred also early in the epidemic of 1889. A young, healthy man came to town to spend Christmas with his relatives, who were in an hotel. Within a short time from his arrival he was seized with an overwhelming drowsiness and fever. His drowsiness was indeed so great that he could by no means be kept awake, and in this respect the case corresponded to a mild attack of the sleeping form of influenza as it has occurred in this epidemic, and has been recorded as "nona" by Braun and others (1).[1] He was removed to a nursing home because of some slight roseola which suggested scarlatina, but within a few hours he was so prostrate, with so much subsultus, and a tongue so dry, brown, and cracked, that he presented the appearance of some severe form of continued fever. There was somewhat of the dusky appearance of a case of typhus, the engorgement of lung either of that or of enteric fever, the pulse about the ordinary rate of typhoid; but the pyrexia did not run the course of either of these, and in five or six days the fever had spent itself and the man was convalescent.

Another group may well be styled "pulmonary influenza," for the violence of the disease expends itself chiefly upon the respiratory tract. There is the same sudden attack, with the aching head and limbs, the fever, the thickly coated tongue. But the cough is more troublesome, there is more obvious impediment to the respiration, and the posterior parts of the lungs are full of sharp, sticky rales of a quality quite peculiar to the disease. This condition will often slowly increase, and extend over the lung, the fever continuing, and the breathing of the patient becoming more and more embarrassed. Delirium supervenes, the pulse at last mounts up, and the case terminates fatally, without, so far as the physical signs go, any evidence of consolidation being at any time present. Sometimes in the course of the bronchial catarrh patches of solid lung will appear here and there, or an acute pleuro-pneumonia will suddenly light up. In some of these the influenza bacillus has been found, thus showing the disease in truth to be influenzal pneumonia; in others, again, only the pneumococcus, giving support to another contention that the consolidation is in some cases a sequel or complication, and not the primary disease.

When pleurisy occurs it often runs on into an empyema. In most

[1] See also p. 946.

cases, happily, the catarrh, though slow in taking its departure, gradually becomes of a less glutinous quality, and the expectoration more and more free, until the amount of the purulent discharge expectorated becomes so excessive that one wonders where it can all come from, seeing that there are seldom any physical signs adequate to so profuse a flux. Sometimes the pulmonary affection leads to hæmoptysis, occasionally profuse, and to hoarseness, and may thus have much superficial likeness to tuberculosis. Into this—the pulmonary form—the simple or common influenza often passes. There is often, indeed, a much quickened respiration, even when there are no physical signs of any pulmonary disease, and Graves (quoted by Thompson (14)) describes a dyspnœa which is not to be explained by any stethoscopic signs. Over and over again, too, there is the history of three or four days of fever, then a return to a normal temperature and apparent convalescence; and then, after perhaps twenty-four or more hours, a relapse, not infrequently ascribed to some indiscretion in uncovering or what not, but which, in most cases, is probably a part of the disease. And with the relapse come more pulmonary symptoms—more cough, more expectoration, more fever, a gradual and too often uncontrollable invasion of the lung by the glutinous bronchitis already described, and in too many cases death eventually by the delirium and the exhaustion of a gradually asphyxiating bronchitis, or of a pneumonia that knows no crisis.

Even when the disease clears up it is very slow in its progress; the expectoration remains profuse and purulent; the lung is slow in expanding to its full extent again, and, until it has completely recovered, is very prone to temporary recurrences of the old physical signs.

Both in respect of the fever and pulmonary complications influenza is a markedly relapsing disease. I have many a time noted that a relapse has taken place after an interval of eight or ten days from the subsidence of the initial fever.

Influenza that spends itself primarily and chiefly upon the heart is not a common occurrence, but it is a very grave matter when it does happen. The symptoms are a frequent and alarming tendency to syncope, and a feeble, irregular, and often a very rapid pulse.

A waiter, æt. thirty-five, who had drunk freely, was suddenly taken ill with influenza. He kept at his work as long as he found himself able—a matter of a day or two only—and then sent for his doctor. His state was as follows: He was a well-nourished man, sitting half upright in bed, with a short, panting respiration and slight lividity of the lips. His pulse at the wrist was hardly perceptible, though regular, 120 in the minute. His general condition reminded me most of cases of severe pericardial effusion, but there was no evidence of any increase of the precordial dulness, nor were the sounds muffled in any way. The impulse was diffused and palpable beyond the nipple, the first sound was metallic and flapping in character, but there was no murmur. The other viscera were in good order. The only conclusion that seemed possible was that an acute dilatation of the heart had taken place, and the man was so ill

that he appeared likely to die. As a rather forlorn hope strychnine was injected subcutaneously with much apparent benefit, and he recovered.

The signs of cardiac failure are for the most part a ready tendency to fainting, a feeble, irregular pulse, sometimes pallor, precordial distress or pain, and sweating. There are records of a fatal issue in such circumstances, sometimes sudden, like the paralysis of diphtheria; at other times deferred for a few days, after the manner of acute dilatation of the heart. For example, a middle-aged man of very nervous temperament was taken ill with influenza. He was kept in bed and had no alarming symptoms, but as he flagged and was depressed he was told to get up. In the exertion attendant upon the effort he was seized with most alarming faintness, from which it was difficult to rally him—indeed, he never did rally thoroughly, for his hands and feet remained cold, his face was a dusky grey, his pulse beat 140 per minute, and was very feeble, the first sound of the heart was so feeble as to be hardly audible, he was constantly sick, and he died in about thirty-six hours.

When recovery takes place from attacks of this kind the heart may yet be long in returning to a natural action, the pulse remaining feeble, intermittent, irregular, or easily disturbed; and Dr. Sansom has recorded cases of persistent tachycardia. The pulse is sometimes unnaturally slow as well as intermittent or irregular—40 to 50 per minute only—in this also showing a striking likeness to one of the ominous signs in diphtheria.

As an affection of the circulation thrombosis of one or other of the larger veins of the extremities may here be mentioned. I have seen seven cases of this complication which occurred in all the cases before convalescence had set in, but in some, probably in all, the fever was a long one; this feature, occurring in the second or third week of the disease, helped in two or three cases to determine the real nature of an otherwise indeterminate fever.

Passing next to the more strictly nervous phenomena of influenza we are confronted by the most bewildering as it is the most interesting feature of the disease. And surely of these the suddenness of onset is both the earliest and most striking. A medical man went to bed in his usual health, as he thought, and getting up during the night to void urine, he fell to the ground, and was so weak that he was unable to get into bed again without assistance. Another man was out in his dog-cart driving and quite well. He suddenly fell out insensible. He was picked up, got into the cart and drove himself home; but although he had broken a rib he remembers nothing about the drive, and when he arrived was so dazed that he wanted to get into bed with his boots on, and was thought to be intoxicated. Many similar and even more striking instances might be given of the extraordinary rapidity with which strong men were instantaneously laid low; but these must suffice.

Then there is the intense headache; the extreme prostration, quite out of proportion to the severity of the fever; the drowsiness, occasionally extreme—a man whom I saw went into so deep a sleep for forty-eight hours

that I called it coma without stertor, but when he woke after two days, he was quickly quite himself again: the occasional maniacal delirium of the onset, or, it may be, even definite symptoms of meningitis; the marked mental depression that marches with the disease or follows it. Neuralgia, too, is very common, sometimes mapping out the distribution of certain nerves, and followed by paralysis or other evidence of neuritis; sometimes attacking organs and producing, for example, pain in the eyeball, chest-pang, nephralgia, neuralgia of the testis. Then there are the racking pains in the bones—pains indeed almost anywhere; subjective sensations of all sorts and in all parts, for this short summary is bald indeed in comparison with the multitudinous effects described by the many who were affected.

Of the disease as it spends itself upon the abdominal organs, it will suffice perhaps to say that in one of the later recrudescences of the 1889 epidemic there were a fair proportion of cases in which the chief symptom was of choleraic character—the attack being ushered in by a profuse watery diarrhœa. A gentleman who lived upon a well-appointed flat, and, therefore, had everything handy to his convenience, related that his attack was so sudden, so urgent, and so profuse, that it was impossible for him to retain his control over his sphincter, and that in the few yards between his room and the water-closet a stream of fluid poured from him. Dr. Simon of Birmingham has put on record a series of similar cases, abdominal pain and collapse being added to the liquid discharges in true cholera fashion. But not only so: abdominal influenza puts on many forms. It may be associated with violent sickness; with complete anorexia; with the most distressing and indescribable sensations of "gone-ness" in the region of the great abdominal ganglia, with flatulent colic, with aches and pains in which all the processes and stages of digestion would seem to be laid bare to a quivering brain. Of other less common modes of onset it is less necessary to speak, for it is quite impossible to mention all the vagaries of the attack of this most searching disease; but I have heard of a series of cases all of which presented hæmaturia; and many cases have commenced with sore throat, or acute pain, swelling, and abscess in the ear.

And now before dismissing the primary disease, and passing on to conditions that may with some propriety be called sequels, there is good reason for taking the leading phenomena of the attack as here enumerated, and considering them a little more in detail.

Of the *suddenness of onset* enough has perhaps been said. It is so sudden in some cases as to be instantaneous, and the completeness of the prostration by which it not only, as it were, flings strong men down, but keeps them under, is a thing that appears to be almost peculiar to the disease. Only in cholera Asiatica is the collapse anything like so sudden and continuous, and herein it is due, perhaps, not so much to physical weakness as to retardation of the circulation and the mental hebetude entailed by it.

The *headache* is of an unusually severe character. Descriptions of it

vary, but it is mostly frontal or orbital, and of that terrible kind that forbids sleep and goads the patient into delirium. It is very like the bad headache that ushers in many a case of typhoid fever; but it seldom lasts so long, and usually subsides after two or three days, often earlier.

The *aches and pains* in the bones and general soreness, in like manner, are very severe; sometimes they are like the pain of a breaking bone; sometimes they resemble not a little the lightning pains of tabes dorsalis; sometimes there is a more general ache and soreness in head, shoulders, loins, thighs, that forbid ease in any position and give rise to an indescribable unrest. Fortunately, as with the headache, the pains do not usually last in any severity over two or three days.

The appearance of the *tongue* is often quite characteristic. With occasional exceptions, such as have been mentioned, it is tremulous, large, soft, indented by the teeth, moist, and uniformly coated with a thick, perhaps rather dirty, creamy fur. This is usually associated with a peculiarly offensive fetid odour of breath, which one cannot attempt to describe. Indeed, who should attempt to describe a smell unless there be an easily recognisable odour with which to compare it? The chief characteristic of this influenza smell is its overpowering nastiness. The odour of the sweat of influenza has also been described as peculiar—peppery, mousy, fusty, or mouldy (8).

Of the *pulse*, the most distinguishing characteristic has seemed to me to be that for the severity of the illness it seldom undergoes any proportionate acceleration. A sharp fever with a pulse of only 80 or 90 is quite a usual occurrence. Others have, however, described the pulse of influenza as quick. No doubt it is sometimes, but I believe the more usual condition to be as I have described it, and that in this respect influenza resembles typhoid fever.

Coryzal symptoms are sometimes severe, but they have not been a predominant feature in this epidemic. Probably they were more often in evidence in the earlier part of the outbreak than in its later years.

The *cough* no less has features of its own. It is hard, dry, and racking, and does not ease itself by its occurrence. It often comes on in violent paroxysms, suggestive, as some have said, of whooping-cough, and with the headache, often existing meanwhile, gives rise to the most intolerable disquiet. It is not accompanied by any expectoration to speak of, and it is exceedingly intractable to remedies. From one to another went the question—What is the best remedy for the cough of influenza? and the common experience seemed to be that no drug could be relied upon.

Passing next to the *fever*, it has no very definite type, and unless disturbed by any complication, pulmonary or other, it does not usually run to any unusual height. Its duration is variable; in many cases not more than three or four days; but in many also it would run ten or twelve, or even more. In not a few it ran the twenty-one-day fever of typhoid very close. It might be said by some, and I should myself hold,

that the fever is also very liable to relapse, but this may not perhaps be strictly true, for this relapse is almost always associated with the occurrence of some complication, even though, as I should certainly contend, such complications—pneumonia, for example—by their frequent occurrence show themselves to be a part of the disease. It has been asked by some whether influenza is ever an apyrexial disease. There can be no doubt that it is so sometimes, as virulent forms of other infectious diseases may be. A lady in the height of one of the outbreaks came to feel so exceedingly ill that she was obliged to take to bed. She had excessive headache, and neuralgic pains in various parts of the body, and was ill for many days, and much depressed for some time afterwards. Her temperature was below normal all the time. My colleague, Sir Samuel Wilks (15), records, amongst several others, the case of a gentleman, with whom he is well acquainted, who suffered severely, and was many weeks ill with influenza, yet who had no fever at any time. A very well-known and able practitioner of my acquaintance in the provinces even contends that "typical influenza" has no fever. It is not possible to accept such a statement of influenza in general, but it is possible that it may be true for a special locality or a special period of an outbreak. At any rate, the observation is of importance as bearing upon the general question, and the point cannot be contested. And why should it be? Contagious diseases are by no means wanting which show a similar peculiarity. Cholera is one; but the most comparable is diphtheria, a disease mostly associated with pyrexia, but in which pyrexia may be quite absent, and that without allowing thereby of any more hopeful forecast. Any poison specially noxious to the nerve-centres may so alter the natural heat-regulating processes as to appear upon occasion as an apyrexial disease. That influenza is a malady that expends its force largely upon the nervous centres cannot at this date be denied, and it is equally certain that it may strike, and strike hard, and yet the sufferer be free from fever throughout the malady [*vide* arts. on other Infections].

Another common and characteristic symptom, at any rate after two or three days have passed, is the occurrence of drenching *sweats*. They are variable in severity—to judge from the descriptions of the sufferers—from a peculiarly unpleasant feeling of cold down the back, up to the most profuse sweats. Moreover, as with other features of the disease, they are very obstinate in their tendency to recurrence, and many are the cases in which this symptom outlasts all the others, and, indeed, only gradually dies out after many weeks, or even months.

The occurrence of rigors is another characteristic that may be coupled with the sweats, because it emphasises the likeness of this disease to those of malarial origin—a likeness that has shown itself from the earliest days of the history of the disease when ague and influenza appear to have been considered in common. So far as my own experience goes, I think it may be said that hitherto, and until the occurrence of the late epidemic, we of the present generation were unfamiliar with severe and

repeated rigors, except as the heralds of acute disease or of true ague, or of localised suppuration in this or that part, for example, in the cellular tissue or liver. But influenza introduced us to another common cause of rigors, and severe and repeated shiverings which, before 1889, would certainly have been taken to indicate the formation of pus, have now to be considered from a wider point of view. I have several times known of rigors so severe and so repeated, and the patient to be so ill, as to give the appearance and the subjective sensation of impending death; that one could not but surmise the case to be one of virulent septic poisoning, or of the local formation of pus; and yet, after provoking this diagnosis, the symptoms have disappeared without any such untoward result. I have known of three cases, at least, in which daily recurring rigors lasted over several weeks without any local disease maturing to explain this.

Yet one more sign may be insisted upon, because I have repeatedly found it of value in diagnosis, namely, the extensive diffusion over the bases of the lungs of characteristic *sharp, sticky rales.* It is a pity that no verbal description can convey an idea of the peculiarity of this feature of the disease. It will occur to many that the bronchitis of typhoid cannot be very different, and yet any one familiar with the pulmonary sounds in the two diseases would surely bear out the statement that the two conditions are distinguishable by the ear. In typhoid fever the abnormal sounds are chiefly sibilant and musical wheezings, with no great amount of rale. In influenza the rales are of medium size, sharp in quality, and conveying the idea of a peculiar viscidity of the contents of the smaller bronchial tubes. And the clinical course of the pulmonary affection is quite in accord with this presumption of the nature of the diseased product. For in many cases the mucus cannot be expelled, and it may be long before there is any expectoration. And for the same reason the lung may be long in returning to its healthy state. In many cases, indeed, here was one of the chief dangers of the disease; the mischief crept from some small area at the base of one lung over a larger and larger area of that lung, and then to the other lung, without showing any sign of giving way; in not a few cases the patient was slowly choked by the spread of an exudation or secretion, with the formation or expectoration of which medicine was quite powerless to deal.

And now to pass to the **after-effects of influenza**: I can hardly do better than set out with the words of a layman who, in describing its effects, said, "It hit me hard, for it ridged my nails." As with the initial symptoms of the disease, so with the sequels, the general prostration may well take precedence of any other more definite nerve-lesions. For of all the complaints that are made there is certainly none more common than this: "I had the influenza, and have never been well since." It may be that the sufferer complains of frequent headache; but more often of a feeling of constant "good-for-nothingness," an everlasting sense of fatigue, both of body and mind; to move is an exertion

that is almost insupportable, and is followed by profuse sweats; all power of sustained thought is gone. Sir W. Gowers has well described this state of things. "It is," he says, "an intense feeling of inertia. Every action, physical or mental, requires an effort of the will to initiate and maintain it that is almost painful. Immobility of mind and body alone seem possible, and yet even rest has to be endured, for it brings no freedom from the sense of prostration. So strange and unfamiliar is the state that it seems at first as if it would be only transient, and would be gone to-morrow; but the mistake is realised when day after day, week after week, passes without relief. In perhaps the majority it is only after some months that the natural freedom of untrammelled effort is regained." To this may be added that even now, many years after the original outbreak of this the latest epidemic, there are those who still suffer more or less from sensations such as are here described.

Again, frequent is the case where peculiar "all-overish" attacks have repeatedly seized the man or woman; sometimes flushings, sometimes indescribable internal sensations, but in all cases associated with such a dread or panic of impending death that, as several persons have told me, they would far sooner die outright and have done with it.

Of more definite disease of the nervous system I have myself seen several cases of temporary *mental aberration*, and Althaus collected many cases of all kinds, from simple hypochondriasis to melancholia, mania, and general paralysis. Suicidal temptations seemed especially to follow influenza. Cases of this sort are observed after other severe febrile affections—typhoid fever, for instance—but after no one can it be said that such an occurrence is anything like so common as has been our experience in influenza. But we are not dependent upon what may be called functional maladies such as these, for there have been cases of acute meningitis, for example, during the recent epidemic which have afforded presumptive evidence of being related to influenza. Or if such cases as these allow of doubt, there are other acute lesions of spinal cord and nerves which have been recorded in considerable number. *Neuralgia*, of one distribution or another, has been noted in any number of cases; and of still more serious lesions, Dr. Buzzard met with a case of acute *multiple neuritis* which terminated fatally. Sir W. Gowers alludes to cases of neuritis, and also to the curious circumstance that disturbances of sensation appear to be less common in this form than in that produced by other toxic agents. Sir. W. Gowers also notes that influenzal neuritis appears more prone to attack the face than other forms. A case is quoted from Westphal, where a man aged twenty-five, on the eighth day of convalescence from a sharp attack of influenza, found that his limbs were becoming weak. The loss of power rapidly increased, included all his limbs, and extended to both sides of his face. The nerve-trunks and muscles of the trunk were tender, and the muscles quickly lost faradic irritability, but preserved voltaic—the reaction characteristic of nerve-degeneration. There was but a slight disturbance of sensation. When the loss of power had

reached a considerable degree it was accompanied by the peculiar œdema of the extremities, often met with in multiple neuritis. Then the palsy ceased to increase, and after two weeks more began to lessen—at first slowly, and then rapidly; and went on to complete recovery. Prof. Clifford Allbutt tells me of a case of peripheral neuritis of the lower extremities, in which the gait resembled that of locomotor ataxy; the knee-jerks, however, remained. I have myself seen two cases of paresis of the lower extremities associated with muscular wasting, and have seen or heard of many cases of local wasting of groups of muscles that indicated a localised neuritis. A very interesting group of this sort are the ophthalmoplegias. Of the external group the external recti appear to be the most often affected. Of internal ocular palsies loss of accommodation has been described, and is said by Althaus to be very common: this is one of the several points of resemblance between this disease and diphtheria. Many other ocular troubles have been described in influenza; chief of them is neuritis of the optic nerve or of its sheath, followed by optic atrophy and blindness. Ulceration of the cornea was not very uncommon (Higgens), and, in thus mentioning the loss of sight, one may link with it also a loss of smell sometimes complained of, and still more often a loss of taste that lingers long after the disease has subsided.

Besides these conditions changes have been recorded, both at home and abroad, that have not usually been attributed to any toxic agency, such as we suppose this disease to be. Of these is *acute myelitis*, occasionally localised, but more usually disseminated through more or less of the spinal cord. Even more chronic changes still are said to have followed it, such as locomotor ataxy, spastic paralysis, and so on. It is said that these serious lesions are more likely to occur in the later of repeated attacks than in the first, and it is certain that they bear no relation to the severity of the attack. The post-influenzal, like the post-diphtheritic nerve-lesions, may be just as severe after mild as after severe attacks. Sir Samuel Wilks, in respect of this very point, contends that we have no right to call many of these nervous phenomena "sequelæ," for, inasmuch as in many cases they are the only symptoms, they are the essential disease. As another sequel *diabetes* may next be mentioned, not because it has been common, but because of its nervous origin: Dr. Saundby has described post-influenzal diabetes, so also has Eischel, and I have myself seen cases. Sir T. Grainger Stewart asserted that a considerable number of cases took origin after influenza, and that in a considerable number of those already diabetic, coma supervened as the result of the intercurrent malady.

Of the *pulmonary sequels* pneumonia was the most frequent. That it is often an integral part of the disease has already been said, but in many it was probably rather a sequel, the influenza bacillus being absent and the pneumococcus present. It is necessary, therefore, to suppose, as I shall presently say of typhoid fever, that the influenza in some cases laid its victim open to an attack of pneumonia.

In another large number of cases this seemed certainly true as regards pulmonary tuberculosis. Many a case has seemed to start from an attack of influenza, and many a case of phthisis has been certainly sent on its way with an alarming increase in the rapidity of its progress. Asthma, though in nothing like the same degree, is another malady that has in some cases been definitely traced to an attack of influenza; and in two instances I have known it to be the initial symptom of the epidemic disease. There is also no doubt, too, that empyema is unusually prone to follow upon the acute pulmonary inflammations that arise in influenza. Probably the same may be said of pyo-pericardium. I met with four cases in the height of the epidemic, and I shall also state my strong belief that *infective endocarditis* was no uncommon outcome; at any rate it has seemed to me to be disproportionately frequent during the epidemic, and in the many sporadic cases of fever resembling influenza in these sixteen years that have followed it. A woman with mitral disease in Guy's Hospital took influenza, and thenceforward remained feverish, and died, after several weeks, of malignant endocarditis with infarctions in the spleen and pneumonia.

The mention of unhealthy inflammations of this sort may well lead on to the next sequel that was very common, namely, the formation of *abscesses* in various parts of the body. Many were glandular abscesses, but not all. Abscesses in the brain, in the lungs, in and about joints, in the neck, axilla, groin, have all been met with, and, at one period of the epidemic, otitis of the middle ear and abscess following upon influenzal sore throat was quite a common occurrence. Suppuration in the antrum of Highmore is a distressing and possibly fatal sequel which for a time may escape diagnosis.

These are the main results of this strange and terrible disease. But the list is by no means exhausted. There would appear to be no organ or tissue that may not become the subject of its attack. Dr. Boulting tells me of four cases of *myxœdema* that he believes to have been consequences of attacks of influenza, and acute thyroiditis was twice recorded (in the *British Medical Journal*) during the year 1895 as a complication of influenza. *Purpura hæmorrhagica* deserves mention. Dr. Sansom has recorded a case associated with *acute pemphigus*, and Professor Allbutt tells me of another that occurred in a severe case of influenza with pneumonia and recurrent attacks of mild mania. The patient was a gentleman of forty-five, over the trunk of whose body, though chiefly towards the back, whereon he lay, were very black, close-set petechiæ, that took many weeks to fade. A variety of erythematous eruptions upon the skin have been noticed; and albuminuria and hæmaturia were not uncommon with *nephritis* as an occasional result. *Orchitis* has been noticed in one or two cases.

Lastly, one may notice the persistence, long after the disease has spent itself, of a *subnormal temperature*, a condition that may be taken to mean either the long-lasting influence of the disease upon the nervous centres, or no more than the dyspepsia, the neuralgia, the general "good-

for-nothingness" which are expressive of the severity of the illness the sufferer has passed through. And in this regard may be mentioned two other curious results of the disease that are to be explained, one may suppose, in the same way: one is the development in some people of an *unnatural appetite*. A friend tells me that for a long time after the attack, though habitually a small eater, and taking next to no food in the middle of the day, he would eat four enormous meals; and if from stress of work he was unable to get food, he would suffer such intolerable agony in his stomach that he would rather have died. The other point is the toleration of alcohol that followed the disease in some persons. A young man told me that he was so weak after his attack that he daily took a quart of stout at his lunch and another at dinner, and "it never seemed to go anywhere," nor did he experience any ill effect. An old lady, who in ordinary circumstances was a small eater and seldom took alcohol in any form, had a mild attack of influenza and then a relapse with diffuse phlegmonous cellulitis of one leg. She now took food in large quantities, enough, it was said, for three men, so as to be the astonishment of her friends; and she took twenty-five ounces of brandy, two-thirds of a bottle of port, and a pint of champagne in the twenty-four hours for ten days or more consecutively and made a good recovery.

Etiology and Pathology.—It is a matter of doubt when the disease that we now call influenza first appeared in England. In the sixteenth and seventeenth centuries ague and influenza were not adequately distinguished. The notion of ague, as Dr. Creighton remarks, was uppermost, and there were no means of distinguishing one disease from the other. In the eighteenth and nineteenth centuries the idea of catarrh has been the more prominent.

But it would seem probable that since 1650, or thereabouts, a disease of the same characters as our visitant of recent times, or approaching thereto, has now and again appeared in this country. This, however, would hardly be supposed from the various appellations given to it. Some of these, as narrated by Dr. Creighton, are as follows: In 1562, "the new acquaintance"; in 1580, "the gentle correction"; and at later dates "the new delight," "the jolly rant." There can be few indeed, having had experience of our recent epidemic, who would not rather subscribe to the propriety of the term "knock-me-down fever" (applied sometimes to dengue) than speak of it thus tenderly as "the gentle correction," and still less as "the new delight." Happy are we if with our recent and vivid memory of such a scourge we can yet smile at the conceits of a bygone day.

So far as the attack itself is concerned, the description of the epidemics of earlier times is wonderfully accurate now. Subjoined is a description by Huxham of the disease as it appeared to him in 1733 (2): "It began with slight shivering, followed by transient erratic heats, headache, violent sneezing, flying pains in the back and chest, violent

cough, a running of thin, sharp mucus from the nose and mouth. A slight fever followed, with the pulse quick, but not hard or tense. The urine was thick and whitish, the sediment yellowish white, seldom red. Several had racking pain in the head, many had singing in the ears and pain in the meatus auditorius, where sometimes an abscess formed; ulcerations and swelling of the fauces were likewise very common. The sick were in general much given to sweating, which, when it broke out of its own accord and was very plentiful, continuing without striking in again, did often in the space of two or three days carry off the fever. The disorder in other cases terminated with a discharge of bilious matter by stool, and sometimes by the breaking forth of fiery pimples. It was rarely fatal, and then mostly to infants and old, worn-out people. Generally it went off about the fourth day, leaving a troublesome cough, often of long duration, and such dejection of strength as one would hardly have expected from the shortness of the time. The cough in all was very vehement, hardly to be subdued by anodynes; and it was so protracted in some as to throw them into consumption, which carried them off within a month or two."

This description, except in the statement that the disease is rarely fatal except to infants and old, worn-out people—and it is still emphatically true, that to the free liver and the aged the risk is largely increased—would include many of the main features of the disease now. Moreover, there are those still living who experienced an attack in the epidemic of 1847-48, and who having suffered again now, were able to identify their old enemy without any hesitation. Its prevalence has been that of sudden, sharp, short outbursts, mostly exhausting themselves after a few weeks of virulent fury, and then several recurrences at longer or shorter intervals, until at last it has disappeared altogether for ten, twelve, or twenty years. This is how the epidemics have usually been described, and it is the custom to talk of epidemics of particular years—1837, 1848, and so on. But it is doubtful if it be strictly correct so to speak, for if one studies the history of the various epidemics as recorded by Dr. Creighton, each has dragged on for several years, and in some instances there has been no clear interval on paper between one epidemic and another. And surely the history of the 1889 epidemic will still more emphatically tell the same tale. It is now (1905) sixteen years since the epidemic broke out, and I doubt if there has been a single year since in which, in one place or another, there has not been a recurrence of a catarrhal fever—to adopt the old term—which, if wanting in the intensity of the symptoms of the original outbreak, and but very partial in its distribution, has yet presented in one place or another all the old features—nervous, pulmonary, and abdominal—and in some areas has attacked quite a sufficient number of the population to still justify its title to an epidemic. I am not aware that the presence of Pfeiffer's bacillus has been identified in any of these more recent outbreaks, and it is possible that these outbreaks may be no more than the endemic catarrh to which we are all more or less accustomed occurring in those

who have been rendered more susceptible by reason of a previous attack of the true disease. There is some reason for supposing this to be the case, for there are many people who will say that they have had influenza repeatedly since their first attack. Dr. Bulloch, speaking as a bacteriologist, makes a very similar but more positive statement, to the effect that, whereas in the early nineties Pfeiffer's bacillus was frequently met with, it has in recent years become much rarer, although epidemics of catarrh—described as influenza—are still very prevalent. He considers that infections with Pfeiffer's bacilli are rare at the present day, an opinion which has also been expressed in other countries, notably France and America. He believes that what is called influenza clinically is not one disease but a series, caused by different microbes prominent amongst which is the micrococcus catarrhalis.

Personally I am inclined to believe that influenza is still with us. In times gone by, the suddenness of its invasion, the rapid way in which numbers were attacked almost, one might say, at a definite hour, certainly upon a definite day, and the alleged fact that the disease attacked not only those on land, but also appeared upon ships far away from land, and therefore out of all possible contact with sources of contagion, have led to the belief that the disease is one that owns some atmospheric origin. But in the last outbreak the observation that has been brought to bear upon this point has made it certain that the incubation is very short, that the disease is contagious from man to man, that the contagion is carried about by fomites, and that it is by these means chiefly that the disease is spread. For instance, the invasion of a country or district when examined into is clearly not so sudden as has been thought. In the first outburst of the disease in the winter of 1889, the disorder befell us, apparently, almost upon a particular day in the last week in December. But, as I have already said, cases had occurred for several weeks before; and this is certainly true, for on looking over notes of cases at that period I find several in the preceding month or five weeks that puzzled me at the time, but which I now know to have been influenza. So also when the outbreaks on vessels far from land come to be inquired into, not one, in the opinion of Dr. Parsons, is free from the suspicion that there may have been less complete isolation than has been currently reported. Again, the few towns or villages that have escaped have been remarkable for remoteness of situation or natural inaccessibility, curtailing, therefore, within the narrowest possible limits the intercourse between those within and those beyond their borders. On the other hand, in instances too numerous to mention, the disease has apparently started and spread rapidly from the date of a person going from an infected area to either a healthy house, village, or public institution.

Various hypotheses have been suggested to account for the propagation of the disease. Some atmospheric, such as climatic conditions, or air-borne poisons, such as dust by winds. But a careful analysis of many outbreaks seems to show that no season of the year, no condition of weather, seems to be unduly partial to its appearance, or to have any

effect in inducing its subsidence, nor has it followed steadily in the course of any prevalent wind. Again, it has been thought to be derived from a disease in animals that seems to resemble it, or to have been carried here by the passage of migratory birds. But these suggestions, too, fail of probability when carefully tested by the facts at our command. The permanent home of influenza, if one there be, is not yet absolutely certain. The west of Russia seems on the whole to be its most likely source, for it would appear that "La Grippe" figures largely as a disease in Russia in ordinary years (9). This has given rise to another suggestion—that it has been conveyed to us by means of the importation of Russian oats, but there seems to be no real evidence in favour of such a spread. It has been thought by some that the disease is really dengue fever under another name, but this cannot be. The two diseases are no doubt strikingly alike in some general features, but there are also striking differences (*vide* art. on "Dengue"). The natural habitat is an important one. Influenza seems to spare no climate, whereas dengue is a disease of hot seasons only. There are regions, again, where outbreaks of the one and the other have followed each other at such short intervals (8), that if the one disease has offered no protection against the other the occasion has yet offered an opportunity for skilled observers to watch the one disease with the other fresh in memory, and to contrast the two. Perhaps the most marked difference between the two is that dengue is almost invariably associated with a rash, and is often followed by desquamation in large flakes, whilst influenza is but rarely accompanied by an eruption. In occasional cases there has been a rash very like that of scarlatina or measles, and peeling has also been seen too.

The incubation is short. From two to five days is apparently the limit: usually two or three days, and a still shorter period has been alleged. The following case related by Dr. Broster of Wirksworth (11) may be given to illustrate this point:—

Mr. X, a teacher of music, etc., went from North Derbyshire on April 6th, 1891, to Sheffield to see his two sisters, then ill with influenza. He returned on the morning of April 7th. He felt very ill on the morning of April 9th, but struggled through his work, and was completely exhausted by night. On April 10th his temperature was 104° F., and he passed through a typical attack of influenza, with a relapse on getting up too soon. On the morning of April 9th he gave a music lesson to some pupils in Miss A's school; none of these contracted influenza. Later in the day he gave a lesson to Miss B, who began with influenza on April 11th. At another house, just afterwards, he gave a lesson to Miss C, who began on April 11th; to Miss D, at another house, who also began on April 11th; and to three girls at Mrs. D's house, all of whom began on April 11th with influenza. In the evening of April 9th he gave a lesson to a small choral society in a village schoolroom. Five of the members of this class began to be ill with influenza on April 11th. Of the five, at least four had stayed behind after the class in conversation with Mr. X. So far as known the above were all the places or houses visited by Mr. X on April 9th, and no fewer than ten persons developed the disease on April 11th. The only

condition common to all was contact with Mr. X suffering from the malady, and who had previously been in contact with his sick relations at Sheffield. On April 12th the married couple with whom Mr. X lodged were both taken ill with influenza; both had waited on Mr. X on the 10th. Up to April 9th no cases of influenza, to Dr. Broster's knowledge, had occurred in the locality. After April 11th the disease spread rapidly, each infected family being a centre of infection.

Not only is the incubation short, but the infective power of the disease develops early, as might be expected from a disorder so distinctly catarrhal in character; for a like reason it is not surprising that instances are on record where the infective power appears to have remained for many days after the onset of the affection. It is obvious that if the infective agent be largely present in the bronchial secretion as well as in that of the nasal passages, the duration of possible infective power might need to be measured by the continuance of the catarrh, whether it relapse in the particular case or not. In this respect it may be that pertussis and influenza show a resemblance to each other. In making this comparison, however, it is necessary to remember that pertussis is prone to relapse again and again long after the primary disease, and that there is no evidence that the relapses are infective in their nature. It may perhaps be thus with influenza—at any rate in those common cases in which certain individuals are said to have had the disease time after time. The average of time during which a patient has been said to be capable of conveying the contagion has been put at six or eight days.

The shortness of incubation and early activity of the infecting agent are of paramount importance when considering the next question, namely, the epidemic character of the disease. A short period of incubation must enormously increase the rapidity of the spread of any disease that is contagious. But scarlatina is a disease that has a similar period of incubation, and no such sudden outbreaks are known with it. But two important qualifications have to be considered in this comparison. In the first place, scarlatina exhausts the soil and protects its subject against recurrence; secondly, it is more or less always with us. Influenza does not render its subjects immune, if at all, to anything like the same extent; certain persons seem indeed to be attacked, preferentially, as it were, again and again—and even allowing that, as some insist, the catarrhal conditions that are more or less always present at certain seasons are influenza *in posse*, influenza cannot be said to be always with us in any such sense as is scarlatina. It may be asserted, then, that influenza when it comes finds a soil prone to it instead of proof against it, and finds such conditions over a very wide area of the earth's surface. No previous epidemics have prepared man to resist it in any way, even if they have such a power; like a familiar guest, it finds us with open house everywhere. And if to such ready access be added the other factor that, like measles, it infects actively so early that it is at work for this purpose long before it can be recognised, we have a

combination of circumstances that, as Dr. Parsons insists, explains the extraordinary rapidity of the diffusion of the disease, and one that must be carefully considered and appraised before any attempt be made to estimate the nature or the power of epidemic influence.

What additional influence or influences make for an epidemic are still unknown. It cannot be doubted that some such are needed, and that, speaking generally, they must be of atmospheric order. We have knowledge of epidemics of voles, of locusts, of wasps, of certain caterpillars, of the Colorado beetle, of certain blights, depending no doubt upon the conditions of environment of these lower orders of life by which their reproduction has been extraordinarily facilitated. There seems no adequate reason against some assumption of the kind in the present case. Short incubation, early activity of infecting power, and absence of immunity, would all seem to forecast an endemic rather than an epidemic disease: whereas influenza sweeps over the world and it is gone. We can see it afar off, and trace its progress, but can do nothing to stop it; and it smites the sanitarily pure with a severity on the whole much the same as it shows to the rest of the world.

Atmospheric influences no doubt vary considerably within limits, else why should some suffer headache when thunder is in the air, or the corns of others shoot when dry weather breaks into wet? And as in all zymotic diseases, even endemic ones, there are times when the disease is violently active, times when it sleeps and seems almost to disappear, the conditions of its life-history remaining constant all the time, there is no need to labour the proof of epidemicity. We know nothing whatever, and are a long way off the discovery of subtle influences of this kind, but none the less they certainly exist.

Bacteriology.—The main point, however, that has been made in the present epidemic is that influenza is contagious, and action based upon this conviction has many a time limited its spread. Being contagious it is probably a disease of microbic origin, and investigations in pursuit of a specific germ have resulted in the discovery of a bacillus that has distinguishing characteristics. This bacillus, according to Dr. Klein, was first found by Canon, and being found in the blood was supposed by him to cause the symptoms by circulating in that medium. But so many subsequent observers have failed either to cultivate the germ or to produce the disease by inoculation, that Dr. Klein suggests that such bacilli as are found in the blood are mostly dead. Pfeiffer about the same time described the influenza bacillus independently of Canon, and stated that the home of the active germ is in the grey mucus of the respiratory tract, where the bacilli exist in such numbers, that by care in selecting the specimen almost a pure culture may be obtained. This is corroborated by Kitasato and others.

As regards cultivation of the bacillus, Pfeiffer has produced by inoculation in monkeys symptoms similar to those of influenza. Dr. Klein (6) has made numerous experiments by inoculation of the pure culture upon rabbits and monkeys; in only one monkey was any success obtained,

but the juices from this animal when injected into other monkeys produced the disease in some of them. This difficulty of reproducing the disease by inoculation is of importance, because it is believed by some that human influenza exists also in horses, dogs, and cats. There is some evidence in support of the belief, but it is meagre and equivocal.

Thus ((9) pp. 105-6), "The influenza epidemic was preceded or accompanied in London, Cornwall, Staffordshire, and other places by a prevalence of a disease known as 'pink eye' among horses. In London this epizootic preceded the influenza epidemic by about six weeks. In other places, however, the disease among horses followed the epidemic among human beings" (Parsons, *loc. cit.* p. 105). And again, "In many places where influenza has been epidemic, domestic animals, especially those living indoors, as pet dogs, cats, and caged birds, have been noticed to be concurrently affected with symptoms resembling those of influenza or of catarrh, and in a few instances a cat was thus affected shortly before the members of the family were attacked with influenza." But as regards the influenza of horses it appears to Dr. Parsons unlikely that it led to the epidemic in men, because "influenza" in horses has frequently prevailed at times and places where there has been no human epidemic; that in the late epidemic those having to do with horses were not observed to be specially or earliest affected; that apparent transmission from horse to man was of somewhat rare occurrence; and that in many places though the disease prevailed in men, horses were altogether free.

Pfeiffer's bacillus, as it is now called, is very minute—0·3 μ in thickness, not exceeding 1·5 μ in length. It occurs in masses, or singly, or in twos and threes. In stained specimens it has a peculiar appearance, the protoplasm being segregated into a stained granule at each end, while the middle portion remains unstained, and shows only the outline of the sheath. Thus the bacillus looks like a diplococcus, and where two are placed end to end, they look like a chain of four spherical cocci. They are non-motile, do not form spores, and are strictly aerobic. They are found in quantities in the bronchial secretion, and, in severe cases, in the peribronchial and subpleural lymphatics.

Pfeiffer proved that (if the patient died at the height of the disease) the secretion from the smallest bronchi and the patches of bronchopneumonia presented a pure culture of the bacillus. The larger bronchi and trachea might contain the pneumococcus and streptococcus also. If the patient lived longer, then the pneumococci and streptococci, germinating rapidly, might penetrate into the diseased alveoli, and thus a mixed infection was obtained. Dr. Klein (7) fully confirms the statements of Pfeiffer that the characteristic influenza bacilli are constantly present in the bronchial sputum of influenza cases; that in well-marked cases they occur in great abundance, singly, in small groups, and in larger masses, and in some portions of the sputum almost as a pure culture. The results also go to confirm Pfeiffer's statement, that as the disease abates the number of the bacilli also rapidly diminishes. Dr. Klein records two examinations in which the rusty sputum was full of Pfeiffer's bacilli, and that these con-

siderably lessened as a day or two passed by and the disease diminished. Dr. Klein also records that in cases of acute influenza with bronchial expectoration the fluids of the mouth contained abundance of influenza bacilli.

Thus much of the bacillus. It is consistent with all that is known of most of these minute organisms that their presence in the secretions of one part or another should be associated with a specific state of pyrexia in the individual attacked. But we have yet to consider the relation of the germ to the after-effects of the disease, and the explanation of these is by no means free from difficulty. Influenza in its sudden and severe prostration is very like typhus fever; in its disturbance of the nervous centres and tracts it is more like diphtheria. The difficulty in both is that the after-effects may come on when and indeed long after the primary disease appears to have spent itself. Up till recent times no explanation of this phenomenon has been at all satisfactory; but now the hypothesis of the production of toxins during the growth of the bacillus adapts itself reasonably, and it would seem adequately, to such cases. Upon this hypothesis the life and growth of the bacillus leads to the production of a toxin of the endo-cellular class, which is supposed to diffuse out of the microbe, and is then carried into the circulation, gradually to work out the distributed effects which characterise the sequels.

Morbid Anatomy.—The mortality of influenza was so large that much information might have been expected under this head. But indeed our knowledge has not been greatly extended. In all sudden epidemics of the kind the disease is so distributed that comparatively few deaths occur in public institutions where such opportunities can be utilised; moreover, the outbreaks are so overwhelming from the numbers that are attacked that it is impossible to turn aside from the living to the dead. Indeed we have not yet arrived at that certainty which will enable us always to distinguish between the changes in tissues or organs that are due to this acute process or the other.

Thus, speaking generally, the changes in the lung, for example, are those of bronchopneumonia, of acute lobar pneumonia, or of acute bronchitis; yet there are no obvious morbid characters by which, apart from the history of the case, we can recognise such changes as belonging to influenza. It is true in the main that the morbid changes of influenza are the result of certain secondary processes; influenza opens the door, as it were, to various other poisons, which we have already indicated in the clinical description—the streptococcus with the consequent production of pus, the pneumococcus with the production of pneumonia, and so on.

Certain changes, which appeared to be peculiar, have, however, been described in the lungs, not only in the more recent, but also in several of the earlier visitations. I may quote, in particular, from an account of the epidemic of 1837, as recorded by Graves upon the authority of Dr. George Green: "The bronchial mucous membrane was found in every case more or less congested and inflamed. . . . The inflammation

in most cases occupied the trachea and the bronchial tubes of both lungs. . . . A sanguinolent frothy mucus occupied the area of the tubes, and increased in quantity as they were traced to their minuter divisions. The parenchymatous tissue of the lung was invariably discoloured, and it did not crepitate, or very feebly so, when pressed between the fingers. The surface of its section was not rough to the touch, and when pressed in the hand a quantity of the mucus described was driven out. . . . When the torn surface of such lungs was examined it did not appear granulated. . . . The signs of recent pleuritis were rare."

Dr. Louis Hayne, writing of the morbid anatomy of the lungs in the recent epidemics, agrees very closely with this description. He notes the frequency of lobar pneumonia and its tendency to attack the upper lobe. Ribbert of Berlin is quoted to the effect that "the hepatisation on section has a peculiarly smooth aspect, differing from the ordinary granular aspect of acute croupous pneumonia. Sometimes there is marked interstitial inflammation, explaining perhaps the tendency to abscess and pulmonary gangrene. This peculiar smooth aspect has been frequently observed in the deaths from recent epidemics, as has also the association with it of areas of bronchopneumonia. Often the solid lung looks as though it were composed of a number of patches of broncho-pneumonic consolidation, these patches having run together and involved the whole lung, suggesting the appearance of a confluent bronchopneumonia rather than that of the croupous variety of pneumonia. . . . This is often found in conjunction with red hepatisation. . . . In some cases pale patches of bronchopneumonia are scattered throughout the lung so as to suggest at first sight the existence of miliary tubercle. As regards the bronchi, inflammation of the larger tubes is very common, besides the capillary bronchitis, the bronchi being congested and covered with thick mucus. The tubes are generally filled even to considerable dilatation with muco-pus. The whole thickness of the bronchial wall is softened. Sometimes the contents of the bronchial tubes are not muco-purulent, but fibrinous." I cannot myself attribute much significance to this smoothness of surface. I am quite familiar with it as, at any rate, an occasional feature of irregular forms of pneumonia; and it has seemed to me sometimes to be due to a want of intensity in the exudative process, sometimes to the occurrence of mixed forms of inflammation, particularly in the direction of interstitial changes and nuclear proliferation, associated with collapse of the spongy structure of the lung. Little more can be said, and this little is scarcely distinctive. Probably as much could be said of an epidemic of measles. The peculiarity of the changes lies mostly in the fact that acute bronchopneumonia, a rare disease in the adult, is the common morbid change found in the bodies of those who die of influenza, but that it is often associated with patches in which the microscopical changes are those of lobar pneumonia.

Before now quitting the etiology and pathology of the disease, I am tempted to say that epidemic disease has a valuable bearing upon a very interesting question, namely, that of the "change of type" of disease.

In diseases that are ever with us, that grow old as we do and with us, it is difficult, though it might seem easy, to express an opinion upon such a point. For it may easily be with disease as it is with the face of a familiar friend. How easy it is to think that face has altered in little or nothing since the days of our boyhood together! Yet what havoc does the fashion of the day, with its photographs of the individual at various stages of his existence, make with any such fond idea! In influenza, however, we have a disease which only visits us at considerable intervals, and thus it affords a favourable opportunity of eliminating this possible source of fallacy; and it would appear from evidence already quoted that there is no material alteration in the symptoms; as they were in former times, so they are now.

But it is possible that if the causes be the same the individual may have altered. Is there any evidence upon this head? Without answering this question in any decisive way, it may be worth while to point out that there is no record in former times of the long series of post-influenzal nervous disorders with which we are now but too familiar, and which will be found by our successors when in the heat of epidemics yet to come they study as we do to-day the recorded experience of the past. The difference in this respect that can be noticed between the past and present may indeed be due to a simple imperfection in the medical record, and the question must be left an open one; but it may well be considered a chief object of the chronicle of to-day to put clearly on record, that as a disease influenza has shattered the nervous systems of a large number of its victims, in some cases permanently, in many for several years after it has run its course.

Whether this disorder has the power of modifying the course of other diseases may more conveniently be considered under the head of diagnosis now to come.

Diagnosis.—The general symptoms have already been sufficiently considered. All observers have insisted upon the extreme prostration as the typical feature of this disease. This has probably led us into some neglect of one or two other signs that are probably not less weighty as means of diagnosis. Chief of these I would place the thick coating of a moist, dirty, creamy material upon a large, flabby, and often tremulous tongue. To this characteristic tongue must be added the tendency to profuse sweats, a pulse but little accelerated, and a pyrexia, if present, of indefinite type. In the great majority of cases the key to the diagnosis rested upon the accurate fitting or otherwise of one or other of these pieces into the mosaic—in such, at any rate, as presented any difficulty; and these were many. Any number of cases have been seen that at their onset looked like influenza, but which afterwards proved to be typhoid fever; and who can wonder that the diagnosis is occasionally a halting one? A large number of cases of either may each begin with headache, shivering, general aching, and a pulse but little above the natural rate. Sometimes, too, the spleen may be enlarged. How can the two diseases, then, be distinguished until some characteristic development occur?

Watson noticed the resemblance of the early stages of influenza to continued fever. Yet it is possible that a provisional diagnosis of influenza and a final one of typhoid fever was by no means always a mere mistake; and there are those who think that the occurrence of the one disease renders the patient subject to an attack of the other. Such proclivities are well recognised between measles and pertussis; between scarlatina and diphtheria. It may be so here, although where mistake is so easy it might seem unnecessary to apply any such disputable hypothesis. There is, however, the more reason for thinking this to be possible, as there seems some small amount of evidence that influenza, or the conditions of our environment that favour its development, may also modify in various ways the natural course of other diseases. Some examples of this tendency have already been alluded to, namely, the rapid development of pulmonary tuberculosis after influenza, the risk of pleurisy taking on a suppurative form, of an endocarditis assuming a malignant type, of a sore throat leading to an acute suppuration of the middle ear; and I cannot but think that typhoid fever has of late shown anomalous features that may possibly bear a similar interpretation. For example, a young man had been exposed to cold and wet during the prevalence of influenza, and had imperfectly guarded himself against such influences. He was seized with rigors and went to bed, and thenceforth his sole complaint—for he was quite clear in his mind—was that he was constantly drenched with perspiration. His temperature was 104° F., his pulse only 90, his tongue moist and rather creamy, his bowels required some mild laxative. Clearly the disease, although undoubtedly typhoid fever, for he had profuse intestinal hæmorrhage about the twelfth day, from which he rapidly sank, was, in respect of the rigors and sweating, of an influenzal type. Of late many cases of typhoid fever have been associated with inordinate sweating. Another case that I have some knowledge of began with wild maniacal delirium, much more like influenza than typhoid; and other examples could be given where premonitory symptoms of influenza ushered in typhoid fever, and this would seem to be a new experience. That this is no more than a personal opinion I fully admit, but even the opinions of those who have lived through an epidemic of a disease that may not visit us again for many years are worth mention. They must be recorded now or not at all, and they may be useful in the future as suggestions for observation and inquiry.

But difficulties in diagnosis arise in other directions. I well remember seeing a lady who was suffering severe and repeated rigors, which, together with high fever, seemed ominously indicative of hepatic abscess, or some internal source of grave septicæmia. She had undergone a few weeks before some slight operation upon the uterus, but was supposed to have quite recovered, and, as it proved, had done so. Had it not been for the late epidemic of influenza which has enlarged our breadth of view in the matter of rigors, the diagnosis would have been unhesitatingly of a very grave character. As it was, it remained doubtful, and the doubt was solved by the patient convalescing without a drawback of any kind.

One other point may be mentioned, namely, that influenza is often so indefinite in its features that the diagnosis can only be arrived at after the event, if then. And it is probable that this is of importance if any adequate notion of the impact of the disease upon the population is to be obtained. Here is an illustration of the sort of case that was constantly occurring. One member of a family had a sharp, febrile attack of quite indefinite nature. Within a few days another member had earache and double otitis; and then another had otitis, or a threatening of it, and mastoid pain, and this was followed by a troublesome orbital neuralgia. Taking the cases separately there is nothing to justify such a diagnosis, but putting them together, and bearing in mind the intimate relation that exists between influenza and inflammation of the middle ear, it is surely not improbable that the disorder in each case was influenza. To take another case: a man apparently in perfect health, and having committed no indiscretion in diet that could by any means explain it, awakes in the middle of the night with indigestion and diarrhœa. The diarrhœa was a pure watery flux, was associated with slight pyrexia, lasted forty-eight hours, and left the man well, but for him unusually limp and tired. There was no thought whatever of influenza. But, nevertheless, for weeks afterwards he was much troubled with an evening neuralgia of one side of the face; and not long afterwards, after a little excess of work and exposure that in ordinary circumstances would not have done any harm, he was seized again with a bad neuralgia, that woke him regularly for several nights out of his first sleep and compelled him to sit up for the rest of the night. There is surely some ground for suspicion that the initial attack of choleraic diarrhœa was of influenzal nature, and that the neuralgia afterwards was the sequel that made the diagnosis possible.

Two other headings remain to be considered, namely, prophylaxis and treatment, and these, though the most important of all, allow only of a very brief statement.

As regards **prophylaxis** the obvious thing is to keep out of the way of contagion. Where strict isolation has been possible, as in certain institutions, the disease has seldom appeared; most risk of catching the disease is run in public buildings or ill-ventilated rooms of any sort, a railway carriage with closed windows not excepted. It also seems certain that excesses in living of all kinds favoured the inroads of the disease, as also did exposure and fatigue. All observers have testified to the frequency of the disease and to its heavy mortality in the alcoholic particularly, and also in the overworked and harassed.

A large section of the public, in addition to common-sense hygiene of this sort, applied itself to various drugs and inhalations in the hope of warding off an attack. Quinine was in most frequent demand internally, and eucalyptus as an inhalation; but it cannot be said that either quinine or salicin in the one way, or inhalation in the other, showed any positive success.

We are as yet in ignorance how long the influenzal poison retains its vitality, but common prudence suggests that infected rooms and clothing

should be well disinfected and well aired after they have been contaminated.

Treatment.—There is no specific yet at hand for this disease. This is quite certain from the number of drugs that have been regarded as almost infallible by one observer and another. All are agreed, however, that mildness of attack and speedy recovery are best insured by taking at once to bed, and that it is the worst folly to struggle on with work and to attempt to fight the disease,—a plan that, although some come through successfully, is nevertheless the cause of the loss of many lives.

To go to bed, to take plenty of light liquid nourishment and some liquor ammonii acetatis every few hours, was sufficient in most cases to induce a quick recovery. Other remedies largely in request were salicylate of soda in ten-grain doses every three or four hours, antipyrin, alone or combined with the former, phenacetin, and quinine. Upon a review of the whole epidemic, there appears in these drugs nothing of a specific effect in cutting short the disease; but in many cases, by their sudorific action and in the control that they have over the temperature, they were productive of relief, and made for the return of health. For the rest it is necessary to combat symptoms as may seem best: the cough perhaps most readily with opium in some form, codeia, glyco-heroin, and the like; the aches and pains perhaps in a similar manner; and for the long-lasting after effects some of the many good nerve tonics, such as arsenic and the hypophosphites or phosphorus, and the judicious use of alcohol, have been upon the whole most successful.

For most of the statements in the foregoing article I have appealed, in the first instance, to my own experience. But in the preparation of the article I have frequently referred to Dr. Theophilus Thompson's *Annals of Influenza in Great Britain from* 1510-1837; to the *Report to the Privy Council on Influenza* by Dr. Parsons; to the *Further Report and Papers on Epidemic Influenza*, 1889-92, by the same gentleman; to Dr. Klein's report in this latter volume; to a Monograph on Influenza by the late Dr. Althaus; and to Dr. Creighton's *History of Epidemics in Britain.*

The literature of influenza scattered over the periodicals of the last sixteen years is very voluminous; this also has been consulted as much as possible, but the task has been rendered incomparably lighter by such recent publications as those I have specially mentioned, containing as they practically do all the information that is to be obtained upon epidemic influenza.

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J. F. G.

DIPHTHERIA[1]

Etiology and Prophylaxis, by the late Sir R. Thorne Thorne. Revised by Dr. W. H. Hamer.

Bacteriology and Pathology, by the late Professor Kanthack. Revised by Dr. F. W. Andrewes.

Clinical Features, by Dr. Samuel Gee; with a note on Intubation, by Mr. E. H. E. Stack.

Treatment by Antitoxic Serum, by Dr. Herringham.

Diphtheritis and Diphtheria are names which were invented by Bretonneau,[2] in 1821, to denote a certain kind of specific inflammation (*phlegmasie spécifique*). In his endeavours to distinguish diphtheria from other diseases he was compelled to rely altogether upon observations made at the bedside and post-mortem table; nor has any other means of discrimination been possible until within the last few years. Yet the clinical definition has never been adequate to its intention, and, in respect of some cases of sore throat attended by the formation of false membrane, it has always been doubtful hitherto whether they are to be deemed diphtheritic or not. At one time it seemed probable that an adequate definition, based upon the essential cause of the disease (the very *ens diphtheriæ*), could at length be propounded; that diphtheria might be taken to signify disease due to infection by the bacillus of Klebs.[3] But now we know that the bacillus of Klebs and Löffler is not found in some of the cases which we have been accustomed to call diphtheritic, and that certain micrococci have the power of

[1] The history of diphtheria being beyond the scope of this essay, the reader may be referred to the works (1, 2, 4) mentioned on p. 1027.

[2] "Il me soit permis de désigner cette phlegmasie par la dénomination de DIPHTHÉRITE, dérivé de ΔΙΦΘΕΡΑ, *pellis, exuvium, vestis coriacea*" (3) p. 41. (Διφθερίτης and διφθερίας have the same meaning: qui gestat pelliceam seu coriaceam tunicam).

[3] In a book called *Scrutinium physico-medicum contagiosæ luis quæ dicitur Pestis*, by Athanasius Kircher, published in 1659, will be found a remarkable exposition of the doctrine that contagious diseases are dependent upon living particles, contagia viva, semina animata. He frequently refers to *male in canna* (diphtheria) as a kind of pestilence. Pestilential "effluvium est animata fœtura vermium. Sunt autem hi vermiculi pestis propagatores tam exigui, tam tenues et subtiles, ut omnem sensus captum eludant, nec non nisi exquisitissimo smicroscopio sub sensum cadant, atomos diceres."

setting up a pellicular inflammation. So, if we continue to use the word diphtheria in the sense of Bretonneau, we must distinguish several kinds of that disease (bacillary, micrococcal, and so forth); or if we restrict the use of the word to those cases in which the bacillus is found, we must invent new words to signify the other forms of pellicular sore throat. It would probably be the better course not to diminish the extent of meaning of the word diphtheria, and still to use it as Bretonneau used it, but in a generic sense. However, the popular tendency seems to set in the other direction, that is to say, to confine the name to those cases in which the bacillus is found [*vide* p. 986]. Moreover, causes seldom operate singly and simply; and even that diphtheria which is characterised by the presence of the aforesaid bacillus, is apt to be complicated by the action or co-operation of other morbific microbes, so that diphtheria is seldom or never due to a simple infection. Indeed, for practising physicians, the main note of diphtheria is still found in the presence, not of special microbes, but of false membranes upon certain mucous surfaces or upon abraded skin; it being well understood that false membranes are not quite peculiar to diphtheria, even when the word is used in its most extensive sense: the mucous surfaces referred to are those of the throat, nose, and windpipe—not to speak of surfaces seldom affected, such as those of the stomach, conjunctiva, and vulva. Definitions of this kind, though rude and inadequate, serve useful purposes until wrought out into a full description of the disease. S. G.

Etiology and Prophylaxis

By the late Sir R. Thorne Thorne, K.C.B., F.R.C.P., F.R.S. Revised by W. H. Hamer, M.D., F.R.C.P.

There is much to justify Oertel's assertion that diphtheria is "one of the oldest epidemic diseases of the human race." A disease, in description like diphtheria, has prevailed from time to time in various parts of England. It occurred at intervals during the latter half of the eighteenth and the earlier half of the last century; it assumed an epidemic form when the "Boulogne sore throat" occurred on the French coast; and from 1855 onwards it has been recognised as being more or less continuously present in this country. Until recent years available statistics of diphtheria in England and Wales have been limited to fatal attacks; and most of the data, especially the earlier ones, are more or less imperfect by reason of faulty diagnosis and faulty nomenclature. But, such as they are, they show that during the decennial periods, 1861-70, 1871-80, 1881-90, and 1891-1900, the rates of mortality from diphtheria per million living were 187, 121, 163, and 263 respectively. The increase of the rate of mortality from diphtheria indicated in 1881-90 was thus more than maintained in 1891-1900. In the eighteen years 1871-88, the mean of the annual diphtheria death-rates per million living in England and Wales was only 137, the rate hardly ever exceeding 160; but for the eight years

1889-96, the mean of the rates was 240, the rate for 1893, namely 318, being the highest recorded since 1859. Indeed, examination of the mortality returns shows that for rather more than twenty years there has been in England an increase in the recorded rate of mortality from diphtheria; the death-rates from the disease were it may, moreover, be noted especially high during the years 1893-1900 (*vide* p. 60). To some extent this increase may be set down to improved diagnosis, and better methods for the certification of deaths; and it may be observed that it has been accompanied by diminution in the mortality recorded under other headings, and notably in that referred to scarlet fever and to "croup." The increase has, moreover, as will be seen in the sequel, been associated with a distinct change in the age-incidence of the disease. The lessened mortality from diphtheria in quite recent years stands in relation in point of time, and is presumably in part attributable to the use of antitoxin, first introduced in 1894.

It may be convenient at this stage definitely to formulate *certain propositions respecting diphtheria* which may be considered to be demonstrated.

1. Diphtheria is a specific infectious disease, primarily and preferentially affecting mucous surfaces, notably the upper portion of the respiratory and alimentary tracts; also, but more rarely, affecting abraded surfaces of the skin.

2. Diphtheria appears first as a local disease, the part attacked being the seat of an inflammatory process characterised by the formation of a membranous exudate. The system as a whole is secondarily affected, the general disease being a sequence of the local one.

3. Local diphtheria results from the reception at a particular point of the mucous membrane and the subsequent development there of a definite micro-organism — the Klebs-Löffler *bacillus diphtheriæ*, which must be regarded as the essential cause of the local disease. The general symptoms of diphtheria, on the other hand, are largely due to absorption into the system of a chemical poison or toxin, a result of the life-processes of the bacillus.

4. Diphtheria, or a disease *ejusdem generis*, is found in certain of the lower animals, and can be communicated to them from the human subject.

Considerations of the factors which favour diphtheria will involve reference to much that is still obscure; but our present knowledge of its etiology may best be set out by considering its time and space relationships, together with the evidence upon which certain conditions have been regarded as disposing to this disease.

Periodicity.—Dr. Parsons observes that diphtheria "is apt from time to time to attack particular localities in the form of protracted or recurring epidemics; and again, after being prevalent there for a series of years, it may subsequently die out, and the locality then remain for a term of years comparatively free from diphtheria" (1). Since the middle of the eighteenth century four or five major prevalences of diphtheria can be

obscurely traced in this country, those of which the record is especially clear being those which occurred in the late fifties and early sixties and in the early nineties of the last century. Explanation of such waves may be sought in an altered character of the contagion; the "intensity rising and falling at intervals"; the intensification being accompanied by greater severity of attack, greater power of overcoming comparative insusceptibility, and greater power of epidemic diffusion (2). Dr. Adolf Gottstein of Berlin, on the other hand, has attributed the waves of diphtheria prevalence to rhythmical variations in power of resistance of successive generations; the weeding out of the less resistant being accomplished to different extents at different times; and thus, following upon a period of rapid elimination, there succeeds one in which a less resistant stock again accumulates (3). Dr. Gottstein finds support for his contention in observed variations in Germany in the age-incidence of the disease, but somewhat similar variations in this country have been, as will be seen later, interpreted differently. Finally, explanations of the waves of prevalence may be sought in some change in the external conditions of life, such, for example, as that to be alluded to in connexion with rainfall.

Topography, Soil, etc.—It was shown by Dr. Longstaff that, during the twenty-six years 1855-80, the greatest incidence of death from disease registered as diphtheria in this country took place on our eastern coast, namely, in Lincolnshire, Norfolk, Sussex, and North Yorks; that next in order came East York, Extra-Metropolitan Kent and Essex, counties which are also on our eastern coast, together with Wales and certain counties within or bordering upon the Midlands; whereas the smallest death-rates from disease thus registered were recorded in Lancashire, Devon, and Somerset on the one hand, and in inland counties such as Bucks, Herts, Northampton, Leicester, and Gloucester, on the other. These data in themselves, apart from other considerations, afford no sufficient indication that one or other portion of England is especially liable to fatal diphtheria; but when they are considered in connexion with conditions of soil, surface, aspect, and rainfall, there is some ground for believing that areas which favour retention in the soil of moisture and of dead organic matter, and are exposed to the influence of cold, wet winds, do tend to the fostering and fatality of diphtheria. But that there are other conditions of equal if not of greater importance is unquestionable; indeed, the distribution of the deaths from diphtheria which Dr. Longstaff referred to as holding good up to 1880, has, by reason of other and more potent influences, undergone modification since that date; the increase in mortality which has occurred since that year has been manifested to a much greater extent in the southern counties than in the north of England, while London and the south-eastern counties have especially suffered. Dr. Longstaff directed attention to the differing rates of mortality from diphtheria in three groups of districts classified by him as "dense," "medium," and "sparse" districts respectively; the "sparse" districts suffered most, the "dense" least, and this led Dr. Longstaff to conclude that "some condition associated with a primitive

form of life" must be operative in causing diphtheria; the altered behaviour of the disease in recent years, already noted, is probably explicable in part as being due to greater facilities of communication and to the increasing aggregation of susceptible children in schools (4).

Climate and Season.—Diphtheria, which closely resembles scarlet fever in geographical distribution, especially prevails in temperate climates. It is generally admitted that season exerts a marked influence on its behaviour. Taking this country as a whole, the death-records over a series of years show that the second quarter of the year exhibits the smallest number of fatal attacks; that there is some increase in the third quarter; that a very substantial addition to the number of deaths takes place in the fourth quarter, when the rate of mortality is at its highest; and that during the first quarter of the year a diminution in mortality sets in. Thus, during the several quarters of the forty-two years 1860-1901 the average weekly number of deaths registered as due to diphtheria in London was distributed as follows: 1st quarter 19, 2nd quarter 17, third quarter 19, 4th quarter 25. But judging from statistics which have now for some years been accumulating relating to attacks, non-fatal and fatal, it would appear that the increase in the mortality at the beginning of the fourth quarter is due to increase of attacks in September; and that a not inconsiderable amount of deaths registered in the first quarter of the year relates to attacks which date from the latter part of the preceding quarter. In short, an increase of diphtheria commonly begins about the second or third week in September, the increase goes on augmenting through October and the greater part of November, and a decline in its amount usually sets in not later than mid-December. According to Mr. W. H. Power, October and November constitute "the well-known season of normal extra-activity of diphtheria." There was formerly observable a second tendency to exacerbation, on a much smaller scale, in the spring, commonly about the end of March or the beginning of April; in correspondence with this there was a tendency exhibited in the curves of "laryngitis" and of "croup" to rise above the mean level at about the same time of year; this small exacerbation in the diphtheria curve has become smoothed away in more recent years. The mortality curve shows some indication of a phenomenon, to be later referred to, which is much more marked in a curve of notifications of cases of diphtheria, viz. a tendency to present a notch or depression in August (*vide* also p. 61).

Drs. Longstaff and Gresswell independently discovered the fact that scarlet fever prevalence appears to be favoured by periods of drought, and Dr. Longstaff showed that other diseases belonging to the "scarlet fever group," in which he included diphtheria, stand in a like intimate relationship with deficiency of rainfall. Dr. Newsholme in 1898, in a study of diphtheria statistics from an international standpoint, noted that epidemics and pandemics of diphtheria recurred in cycles, and pointed out that the disease "only becomes epidemic in years in which the rainfall is deficient," and that "the epidemics are on the largest scale when three or more years of deficient rainfall immediately follow

each other." "Conversely," he adds, "diphtheria is nearly always at a very low ebb during years of excessive rainfall, and is only epidemic during such years when the disease in the immediately preceding dry years has obtained a firm hold on the community and continues to spread, presumably by personal infection" (5).

Sex and Age.—There is some excess of diphtheria in the female sex, but it would appear to be largely due to the greater opportunities of infection in girls and women than in the case of males. The excess in females commences at the age when little girls begin to tend the baby and younger children, whilst their brothers are occupied out of doors; and it is maintained throughout that period of life when women and mothers are engaged in house duties and in caring for the sick. Amongst females also habits, such as that of kissing, prevail to an extent which may account for some excess of a disease that is often conveyed from mouth to mouth. At the extremes of life the rate of diphtheria mortality in females does not exceed that in males.

The influence of age on diphtheria is very marked, whether death or attack be in question. By far the highest rate of mortality is that affecting the first five years of life, and especially during the age-period 2 to 5 years; the period 5 to 10 years ranks next, and it is not till after the termination of the period 10 to 15 years that any substantial diminution sets in. In adult life and in old age the diphtheria death-rate is comparatively insignificant. With regard to the comparative immunity of infants under one year of age from death by diphtheria it was pointed out by the late Dr. D. A. Gresswell, that infants at times develop faucial diphtheria without obvious inconvenience, and that this may be due to the rudimentary character of the tonsils at that age. Speaking generally, and including non-fatal with fatal attacks, it may be asserted that there is a special incidence of diphtheria on the age-period 3 to 12 years. Now it will be at once remembered that the age 3 to 12 years is precisely that during which children are in attendance at the elementary schools.

It was, moreover, noted in 1891 and 1894, by Sir Shirley Murphy, that there had for some years been manifested an increasing incidence of diphtheria upon school-ages as compared with other ages, this tendency having been developed at about the time when the Elementary Education Act became operative, *i.e.* in 1871. On including "croup" with diphtheria similar results to those yielded by the diphtheria figures alone were still obtained. In a later report (1898) Sir Shirley Murphy carefully examined the part played by altered nomenclature in determining the change in age-incidence. The figures he found suggested that some transference from "scarlet fever" to "diphtheria" had taken place, but "irrespective of all questions of change of nomenclature," there was increased incidence on the ages 3-4, 4-5, and 5-10, when the figures relating to diphtheria, croup, and scarlet fever were all combined (6).

School Influence.—The influence of school attendance on the diffusion of diphtheria had been noted almost as soon as skilled inquiry into the

circumstances of this disease was instituted. Thus the importance of the question was demonstrated by Mr. W. H. Power at Brailes in 1876, and in the following year the subject was further studied by Sir Richard Thorne during a maintained prevalence of diphtheria at Coggeshall in Essex. The latter divided the 928 children in the village into age-groups, and then ascertained within each group the relative amount of diphtheria in those who attended school and in those who did not. Under three years of age school attendance was not found to have materially influenced the number of attacks; but in the age-period 3 to 12 years the incidence of the disease was not far from 50 per cent greater on those attending school than on others; and in the age-period 12 to 15 years those attending school suffered nearly three times more than those who were not at school. Similar results were noted in other outbreaks; and, quite apart from age susceptibility, it soon became evident that there were certain circumstances associated with school attendance which promoted diphtheria. Indeed, this is now so generally accepted that restrictions in school attendance often form one of the earliest, if not the chief of the measures adopted by local authorities to prevent the diffusion of the disease. But as the subject was more carefully studied, it became evident that the influence of school attendance was by no means the simple affair of personal infection in circumstances especially favourable to the transfer of disease from one child to another; and a further stage was reached when Mr. W. H. Power investigated a maintained prevalence of diphtheria at Pirbright in Surrey. School attendances were recognised there as serving to diffuse the malady amongst a somewhat scattered population; indeed, in hitherto uninfected households, children between three and twelve years of age, who at a given period were attending school, became affected five or six times as often as children of the same age who at the same period were not attending school. Hence, it was deemed desirable to close the schools on several occasions. It was also seen that attacks of "sore throat," which did not present the typical signs of diphtheria, and seemed often but trivial in their character, served as links between the more marked outbreaks of the disease. Hence, besides resort to measures of disinfection at the school-house and in infected houses, sustained medical effort was made to eliminate from the school, on the occasion of each of its reopenings, all cases of sore throat however mild. Thus it came about that comparison was possible between nine alternating periods of school work and school closure,—the intervals of closure lasting generally for some six weeks, and school operations not being recommenced until all signs of sore throat had disappeared amongst the scholars. "While the school remained open," writes Mr. Power, "in the early months of the year, the rate of attack in children aged from three to twelve, presumably susceptible of diphtheria, but not having the disease at home, was 16·6 per cent of those who were at school, and 3·8 per cent of those who were not. The next time the school was opened the respective rates were 4·8 and 0·0; the third time 7·1 and 2·5; and on the November (the last) occasion, 4·1

and 0·0." The numbers on which the percentages are based were admittedly not large, but it is claimed for them that the indication which they furnish is too uniform to be mistaken. A newly-observed phase of school operations seemed here to have been at work; the bringing together of the school children operating again and again so as to give a serious specific quality to throat ailments which either appeared very trivial or were altogether unrecognised; and this with remarkable and even startling suddenness. Similar experiences were soon recorded by other observers; and definite "explosions" of diphtheria have been again and again reported in connexion with school attendances. School influence has also operated in another way, and this especially at those seasons when diphtheria is least prone to show itself in recognisable form. At such times the unexpected occurrence of one or more severe attacks of the disease has led to the idea that the infection might possibly be lingering among the school children, and in these circumstances there has been found an unexpected and exceptional amount of throat sickness, the true nature of which has been revealed upon bacteriological examination, or failing that by the detection of cases of diphtheritic paralysis amongst some of those who have suffered from antecedent throat or nasal symptoms such as are common in mild attacks of diphtheria.

Sir Richard Thorne addressed to the Epidemiological Society of London in April 1878 a communication (7), in which he stated the conclusion, based upon his own investigations into outbreaks of diphtheria, that in certain circumstances the property of infectiveness appeared to be a matter of progressive development, and that throat illness which under one set of conditions might remain practically non-infective, might under others become specifically infective and, in course of transmission, acquire characteristics not to be distinguished from those of the disease known as diphtheria. This view has since been accepted by a number of medical officers of health and other observers; but it has seemed insufficient to account for the explosive character of some of the outbreaks which have occurred in connexion with elementary schools. On this latter point Sir Richard Thorne suggested that a micro-organism possessing in small degree the property of infectiveness might, under one set of conditions of throat, season, and so forth, require repeated transferences and transplantations from throat to throat before any considerable modification of its morbific qualities was brought about; whereas under other conditions of "throat culture" the stages in question might be reached at so rapid a rate as even to account for occurrences such as those met with at Pirbright.

In his Milroy lectures on diphtheria Sir Richard Thorne summarised the various ways in which school influence appears to be operative for mischief much as follows:—1st, It brings together those members of the community who are, by reason of age, most susceptible to diphtheria; 2nd, The children thus brought together are placed, and remain for many hours of the day, in exceptionally close relation with each other; 3rd, The closer the aggregation and the greater the hindrance to free

movement of air, the greater the risk; 4th, Faulty sanitary conditions of the school-house and its surroundings, and such other conditions as tend to a condition of general ill health, in so far as they induce sore throat, favour the reception of any imported diphtheria infection; 5th, There are reasons for believing that the aggregation of children in elementary schools constitutes one of the conditions under which a form of disease of particular potency for spread and for death may be manufactured; 6th, The practices of kissing and of transferring sweetmeats from mouth to mouth—practices more common among girls than boys—the joint use of drinking-cups, and the like, must assist in the diffusion of diphtheria amongst school-fellows (8).

Sir Shirley Murphy, whose observations on the altered age-incidence of diphtheria since 1871 have been referred to, further called attention, in 1894, to the fact that "school influence" in giving opportunity for infection from child to child was being manifested in another way. He argued that "any interruption of school life would be indicated by a diminution in the amount of prevalence," assuming school influence to be at the time operative. In Nottingham it had been found by Dr. Whitelegge that far fewer attacks of scarlet fever began on Wednesday than on any other day of the week, owing presumably to lessened opportunity of infection on Saturday and Sunday. Sir Shirley Murphy looked for evidence of influence of the summer holiday, and demonstrated the existence of a marked "August holiday depression" in the curves showing notified cases of diphtheria and scarlet fever; this depression was especially marked on separate consideration of persons of school age (9).

Recent bacteriological investigation has confirmed the suspicion long entertained that children may act as "carriers" of infection without themselves presenting symptoms of diphtheria. Formerly the only available means of detecting the existence of infectious cases was clinical examination of the throat; now, material from the throats and noses of "contacts" is examined with a view to detection of the diphtheria bacillus. This organism is not infrequently found in apparently healthy "contacts," but only quite exceptionally in other persons. Drs. Louis Cobbett and Graham Smith, when dealing with outbreaks of diphtheria at Cambridge and Colchester, advocated, therefore, isolation of all children harbouring diphtheria bacilli; systematic search for such children was instituted, and their detention in an isolation home recommended, until three successive negative results had been obtained on application of the bacteriological test. Drs. Cobbett, Pugh, and others have insisted upon the importance of examining the nose as well as the throat, for, in the condition described by Ravenal as chronic membranous or fibrinous rhinitis, diphtheria bacilli may give rise to little or no constitutional disturbance, and the patient may, therefore, readily act as a "carrier case" (10).

Direct Infection from Person to Person.—Incidentally this has been referred to more than once already. It is probably by far the most

common cause of diphtheria, and as the fauces and respiratory tracts of the sick and healthy respectively are more closely brought together, so is reception of the poison by this means the more likely to result. Young nurses who carry about in their arms little children suffering from diphtheria; relations and others who kiss persons suffering from diphtheria, whether in a recognised form or not; and children who during school attendances are packed closely together, and thus run risk of inhaling the throat or nasal emanations of school-mates having mild forms of diphtheria,—these are the people who run most risk of contracting diphtheria by direct infection.

Fomites.—The infection of diphtheria has long been supposed to attach itself both to premises and to articles of bedding, clothing, and the like; and there are indications to show that in so far as premises are concerned, the faculty of the diphtheria organism for retaining its vitality is distinctly enhanced by conditions leading to dampness—especially dampness of site. Growths of ordinary mould in premises may often indicate such dampness. In a number of instances the evidence of the communication of diphtheria by means of the bedding and clothing of the sick is such that no doubt can remain of the spread of the disease in this way. Again and again the distribution of such articles amongst relations and others has been followed by diphtheria amongst the recipients, and this in circumstances of time, and of previous immunity from any throat affection, that must remove all doubt as to the relation between the two events. To name one instance only, the despatch of a pillow from an infected house to another locality entirely free from any throat affections has been followed within a few days by the onset of fatal diphtheria amongst the members of the recipient family.

In schools the spread of infection by drinking-cups, pencils, slates, and so forth, has been suspected. Dr. Cobbett records a striking instance in which seven out of nine boys, and only one of seven girls, all members of the same infants' class, were attacked by diphtheria, and it was found that the only ascertainable difference between the boys and the girls was, that twice a week the girls were employed at needlework while the boys had a drawing lesson. "It can scarcely be doubted," says Dr. Cobbett, "that it was during their drawing lesson, when slates were used, that the infection was distributed." The same observer mentions an instance in which a pencil used by some children, who used it in turns to score the marks when playing at parlour cricket, and which doubtless found its way then into their mouths, appears to have served to spread infection.

Milk Diphtheria.—One of the most important discoveries of modern times in connexion with the etiology of diphtheria is its relation to the consumption of milk; and it is not saying too much to assert that many occurrences of diphtheria which might otherwise have been set down to other or to altogether unknown causes, have received their explanation since the dissemination of diphtheria by the agency of milk was first demonstrated by Mr. W. H. Power in 1878 (11). Since that date many outbreaks have been traced with the greatest certainty to milk,—the

disease not only having followed the distribution of a certain milk-supply again and again, even when carried to widely different and distant localities, but having been limited at the onset of the outbreaks in those special localities exclusively to persons using the milk in question.

In certain instances the infection of milk by means of the diphtheria contagium must be attributed to the exposure of milk to infection derived from antecedent diphtheria in the human subject. It is unnecessary to discuss at any length the means by which milk can thus become infected. Wherever the throat emanations go, and whether aerially or by means of material adherent to the hands and clothes of others, there will be risk of infection; hence milk may become specifically contaminated whenever the air of the sick chamber has access to it, or where persons in attendance on the sick take part in any dairy processes. In like manner milk may become infected with diphtheria bacilli when persons who are engaged either in the dairy farm or the milk-shop, or who are occupied in any way in the collection and distribution of milk, are themselves suffering from diphtheria in however mild a form. And it has been shown by Dr. Klein that milk, once inoculated with diphtheria bacilli, is an excellent culture medium for the organism even at such ordinary temperatures as 18°-20° C. (64·4°-68° F.).

But the more we learn of milk as a vehicle of diphtheria, the more probable does it become that the infection is much more frequently derived from the cow herself than from repeated specific contamination by the human subject. Thus it has happened that milk from a certain dairy, whatever the locality in which it has been distributed, has served to convey and to keep on conveying diphtheria to the retail customers; and this although all suspicion of antecedent diphtheria or "sore-throat" amongst the dairy hands could be eliminated with a degree of certainty leaving little or nothing to be desired. And this has happened when the milk, which was obviously conveying the infection, was derived from two different dairies situated at a distance from each other, and having little or nothing in common except the transference of cows from one to the other establishment. So strongly has the evidence in such cases pointed to the cow herself, that Mr. W. H. Power felt compelled to consider (as he wrote now some twenty-seven years ago) whether there might not have been "risk of specific fouling of milk by particular cows suffering from specific disease, whether recognised or not" (12). Later it became possible to trace quite conclusively the milk, which conveyed diphtheria, to certain cow-houses in which one or more cows—notably those which had recently calved—had suffered from an ailment that appears to be transmitted from one cow to another, and is associated with certain definite symptoms, including a rise of temperature and a form of eruption on the udder and teats which, when seen in its later stages, has hitherto been commonly regarded by cow-keepers as "chapped teats." This eruption usually begins in the form of vesicles, which rapidly pass into pustules and scabs, or crusted ulcers. At the next stage in the inquiry it was found that a similar disease could be produced in

the cow by inoculating the animal with sub-cultures of the diphtheria bacillus; and when this was done the material derived from the induced vesicles and pustules was in turn found to contain the same bacillus, which could be unmistakably demonstrated by cover-glass specimens and by culture. And, further, the milk of cows thus inoculated was found to contain the diphtheria bacillus in abundance.

These experimental results, originally obtained by Dr. Klein, remained unconfirmed until quite recently, when Drs. Dean and Todd investigated an udder eruption of cows associated with mild diphtheria. These observers found virulent diphtheria bacilli in the udder lesions, and in the milk; they adduced, however, certain further considerations which they regarded as militating against the view that the lesions were due primarily to a specific diphtheritic infection of the cows (13).

In a number of outbreaks of the disease which may now without question be called "milk diphtheria," it has been found that its different incidence on individuals has come to depend, among other things, on their opportunities for consuming the milk in question. Thus well-to-do persons, largely using raw milk for their families, have suffered out of all proportion to their poorer neighbours, who could only afford a small supply, to be used in their tea. And, further, it has been found that stored milk, in the form of cream and still more of skim-milk, has been more potent for mischief than fresh milk—the storage of milk, as, for example, when set for cream, giving opportunity for the development and multiplication in it of the contained specific organisms.

Scarlet fever, like diphtheria, is of course spread from time to time by milk, and it may further be noted that in some of the outbreaks of throat malady, attributed to infected milk, there has been difficulty in deciding as to the nature of the disease in question. This difficulty appears to have been first experienced in an outbreak at Macclesfield and Upton, reported upon by Dr. Franklin Parsons in 1889; and as more recent examples of anomalous forms of throat illness spread by milk, the outbreaks described by Dr. Kenwood (at Finchley) in 1895 and 1904, by Dr. Warry (at Hackney) in 1900, by Dr. Darra Mair (at Lincoln) in 1902 and 1903, and by Dr. Pierce (at Woking) in 1903 may be referred to.

In connexion with the correspondences shown in the behaviour of scarlet fever and diphtheria, when they are regarded as milk-borne diseases associated probably with some cow malady, their similarity of relation to climate and meteorological conditions may be recalled. The difficulty in distinguishing between them clinically in individual cases and in groups of cases may be paralleled by the confusion between them which is traceable in the history of outbreaks of throat ailment occurring during the last 150 years in Europe and in the United States; while within the period of statistics in this country there is evidence that there has been much uncertainty as regards nomenclature. Again, both diseases are largely affected by "school influence," and in both the occurrence of "return cases" has shown that convalescents may remain capable of conveying infection for a protracted period.

Diphtheria in the Lower Animals.—The cow is not alone among the lower animals in being a medium for the distribution of diphtheria, nor is it the only one to which the disease can be communicated from man. Different animals, including pigeons, turkeys, and cats, have also fallen under suspicion; whether the matter be studied from a bacteriological or etiological point of view, however, it will probably be admitted that the case of one animal only is altogether free from doubt in this connexion, namely, that of the cat. There are a number of instances in which human diphtheria has followed on similar disease in cats; and, on the other hand, evidence has appeared that cats have contracted diphtheria from the human subject. Dr. Bruce Low, in reporting to the Local Government Board on an epidemic of diphtheria in Enfield, expresses the opinion that a disease resembling diphtheria which he met with in the cat was in all probability first contracted from human diphtheria, then communicated from cat to cat, and then transferred again from the cat to the human subject.

Writing in 1889, Dr. Klein (14) states "that cats are really subject to an infectious disease occurring in association with human diphtheria"; and, further, that "this disease casually occurring in the cat is very similar to the malady artificially producible in that animal by inoculating it with human diphtheria." We must, therefore, recognise that diphtheria in the human subject may have its origin in disease of a like nature in at least one animal common in our households, namely, the cat (*vide* p. 991).

The Influence of Sanitary Circumstances.—Few questions relating to the etiology of diphtheria have led to more discussion than that which is concerned with determining the influence, if any, of faulty sanitary circumstances on the causation of this disease. The extremes of opinion are best illustrated by two classes of contentions:—First, there are those who, having to deal with diphtheria, find that in the locality or house where it prevails there are certain more or less obvious faulty sanitary conditions; and these persons are content to regard the coincidence as cause and effect. Secondly, there are those who, often meeting with diphtheria where there is no history of exposure to faulty sanitary conditions, have become convinced that the disease can in no way have relation to such conditions. The truth probably lies somewhere between these two extremes.

In considering this question it should be remembered, in the first place, that the period dating from about the year 1870 has been one in which unexampled progress has been made in England and Wales in improving the sanitary circumstances, whether of water-supply, sewerage and drainage, the disposal of refuse and excreta, or dwelling accommodation. It has also been a period in which the general mortality from all causes in this country has diminished from the mean annual rate, for the first five years of that period, of 22 per thousand living, to one of 17·6 for the last five years of the nineteenth century; in which the corresponding rate from the seven principal zymotic diseases, including diphtheria, has fallen from 4·8 to 2·2; and in which the rate of

mortality from enteric fever—a disease known to be intimately associated with bad sanitary circumstances affecting water-supply, sewerage and drainage, and so forth—has fallen from 0·37 to 0·17 per thousand. But during the same period of sanitary progress, associated as it has been with a substantial diminution in the amount of death from the several causes specified, the corresponding death-rate from diphtheria in England and Wales has gone up from 0·12 to 0·27, an increase of 125 per cent; and in London and the large cities the increase has been even greater—it has, indeed, more than trebled. From these facts it would at least appear that the removal of ordinary faulty sanitary conditions has not only not been followed by diminution in diphtheria, but that precisely the reverse has taken place. In the second place, so far as can be learnt, it has hitherto been found impossible by skilled observers—including the medical inspectors of the Local Government Board, many leading medical officers of health, and distinguished foreign epidemiologists, such as Professor Fodor—to identify the use of polluted water-supplies as a cause of diphtheria. In the third place, it is certain that in the vast majority of cases diphtheria is due either to infection from an antecedent case, whether in school or elsewhere, or to infection conveyed through milk; and that, consequently, the balance attributable to faulty sanitary circumstances cannot be a large one. The advocates, however, of general insanitary conditions as a cause of diphtheria lay special stress on the influence of faulty sewers and drains, and of collections of offensive refuse, garbage, and the like; it is indeed to effluvia from such sources that they are disposed to attribute diphtheria. Their contention, therefore, requires further examination.

Diphtheria, as already stated, is due to a specific bacillus, but this organism has never, it appears, been discovered in "sewer air." Indeed, such experiments as have been made in this direction have resulted in failure. Moreover, it is contended (15) that the micro-organisms found in sewer emanations are related rather to those commonly found in the outer air—being in the main moulds and micrococci—than to the micro-organisms found in the sewage. And further, when, in outbreaks of diphtheria under investigation, some obvious defect leading to pollution of respired air by sewer or drain emanations has been indicated as a probable cause of the disease, it has in almost every instance been found not only impossible to eliminate other and better established sources of infection, but also that there were, as a rule, alternative sources of infection having obvious causal relation to the disease.

But after all has been said in this direction there remains a residuum of cases which cannot so easily be disposed of. These cases are, generally speaking, limited to single attacks, to attacks in single households, or on occasion to a small group of persons having opportunity of infection from the earlier cases. In dealing etiologically with such cases, it is impossible to ignore the fact that exposure to certain foul emanations is in certain persons often followed by sore throat; and it must be admitted that such sore throat, as also the common "household sore throat,"

have infective qualities, although as yet these affections have not been identified with any particular organism. Some persons are extremely intolerant of these and other morbific conditions—such as damp, cold, etc.—and when exposed to them suffer from sore throat; and it is often among such persons that diphtheria may occur almost immediately after exposure to one or other of the emanations referred to. Now a sore throat, however induced, is peculiarly favourable to the reception and subsequent local multiplication of the diphtheria organism. Children subject to chronic sore throats have often been found specially liable to contract diphtheria; and it is also a matter of common observation that convalescents from diseases such as scarlet fever and measles—diseases in which the fauces may be denuded of their epithelial coating—are especially liable to contract diphtheria; whereas it is generally held, though recent fever hospital statistics do not altogether confirm this view, that there is no corresponding liability on the part of diphtheria convalescents to contract scarlet fever or measles. In short, a morbid condition of the fauces affords a soil favourable to the lodgment and maintenance of the diphtheria contagium. Another explanation of the relation between exposure to foul emanations and an attack of diphtheria is, that where the disease has assumed an obscure and chronic form—the local manifestations being mainly nasal or exceptionally mild—exposure to drain emanations, to cold and damp, and like conditions, has almost certainly a tendency to induce and to accelerate the occurrence of those recrudescing attacks of diphtheria which are so fertile a source of the spread of the disease to healthy persons in contact with diphtheria convalescents. But these explanations do not cover a number of cases in which it is, at least, certain that diphtheria prevails concurrently with opportunities for exposure to drain and other like emanations; and some observers, who do not assert that the diphtheria organism is itself conveyed by means of sewer air, contend that there are circumstances in which sore throats, not presenting specific characteristics in their early stages, do definitely acquire them at a later date. When Sir Richard Thorne first suggested that the hypothesis of the "progressive development of the property of infectiveness" was necessary to the explanation of many occurrences of diphtheria, he was inclined to assume that some substantial lapse of time was an essential element in the process. But some observers, including the late Dr. David Page, medical inspector to the Local Government Board, Dr. Fosbroke, county health officer for Worcestershire, and Dr. Jacob, medical officer of health for Mid-Surrey, have recorded instances which seem to indicate that the process may begin and be completed during the stages of a single outbreak of very limited duration. Thus Dr. Jacob records "an outbreak of diphtheria which was preceded for a month by a series of ordinary sore throats," and "gradually worked up, so to speak, to the genuine characteristic form of the disease." Similar phenomena have been noticed in connexion with London school outbreaks (16), and the subject has been referred to by Drs. Wheaton and Reid (17). The possible influence of the age

of those attacked by the disease must, of course, be borne in mind; thus, Dr. C. J. Thomas has pointed out that if a child under five contract diphtheria the attack is as a rule severe, and the child does not remain in school to spread the disease; if, on the other hand, a class attended by children from five to eight years old become involved, mild forms of the disease are more apt to occur, children may attend school with only slight clinical symptoms, and the class becomes a source of danger (18).

In brief, it may be observed:—First, that while the causes which determine variations in diphtheria mortality are ill understood, and that while altered nomenclature undoubtedly confuses the issues, it may none the less be regarded as clear that the available statistics as to diphtheria do not support the contention that the increase of this disease in this country is related to faulty sanitary circumstances; secondly, that the operation of that which is included in the term "school influence" does account to a very important extent for the increase in question; thirdly, that much diphtheria which in former times would undoubtedly have been assigned to faulty sanitary circumstances is now known to result from infection by "carrier cases," or found to be communicated to man through the agency of milk; fourthly, that there are good reasons for believing that sore throats, which are induced by exposure to conditions such as drain emanations, render people especially susceptible to the influence of the diphtheria contagion; and, fifthly, that amongst the residuum of attacks there remain a number in which there is, in appearance at least, a connexion between exposure to foul emanations and diphtheria, and that some of these cases may possibly be instances in which a process of development, even in the same person, leads from a minor affection up to a major and definitely specific disease.

No attempt can properly be made to divide the causes of diphtheria into definite groups. In one sense there is but one cause of diphtheria, namely, the operations of the bacillus diphtheriæ, and the direct influence of this organism has been indicated in each of the sets of circumstances referred to. This is equally the case whether the organism be in a state of specific activity at the moment of its reception, or whether, as has been suggested, it be in a form requiring time and circumstance for development of its specific potency. The real difference between the several sets of conditions concerned in diphtheria is as follows:—Some involve conditions, such as age, antecedent sore throat, dampness of soil, etc., which appear to favour the opportunities for mischief of any chance diphtheria bacilli which may be received on the fauces or other surface; the others, such as direct infection from an antecedent case, infected milk, and the like, involve the reception of the infection in such form, quality, and quantity as practically to ensure the production of diphtheria even where some of those conditions regarded as favouring diphtheria may be absent. Study of the operations of both sets of conditions will indicate the means of prevention.

In the **prophylaxis** or prevention of diphtheria we have to consider

both the general measures which may diminish the chance of contracting the disease, and also the more immediate and active steps which should be adopted to prevent its spread when the disease is actually prevalent.

It is well to remember, and this especially as regards families who tend to suffer from "sore throat," that whilst the broad geological features of a district have not been observed to have any special influence on the development and diffusion of diphtheria, yet residence in localities exposed to cold wet winds, and on sites characterised by constantly recurring dampness of soil and retention of organic debris and other refuse, is, if possible, to be avoided. It is a matter of almost equal importance to secure the influence of sunlight and movement of air about the residences of families and persons who are regarded as exceptionally susceptible to diphtheria. These are points to be borne in mind, especially in the case of old-fashioned and well-timbered country places. The adoption of general measures of sanitation, and especially the removal of those conditions of drainage, and disposal of refuse, which are believed to have some relation to the production of sore throat, should always be insisted on.

Avoidance of infection through the agency of milk can only be ensured by habitual abstention from the use of any milk that has not been previously scalded or otherwise cooked. Fortunately we know that exposure of the diphtheria bacilli to a temperature of 60° C. (140° F.) for five minutes suffices to destroy their vitality. Recent scalding, therefore, gives ample protection against diphtheria through the agency of milk, and indirectly will tend to prevent infection from other contagia, such as those of scarlet fever, enteric fever, epidemic diarrhœa, and tuberculosis.

Ailing domestic animals, notably cats, should be avoided. The evidence of the communication of diphtheria from the latter to man does not admit of doubt.

Diphtheria being a highly infectious disease, easily communicated from person to person, and this at distances the limits of which cannot as yet be stated, the immediate isolation of the infected person should always be attempted. The most effectual form of isolation consists in the removal of the individual to an isolation hospital; but where this is not practicable the nearest available approach to isolation should be secured. Thus, the removal of a patient to the upper story of a house, when that story can be exclusively reserved for the patient and the necessary nurse and attendant, may suffice, provided strict precautions are taken to maintain the isolation. The apartment of the patient should be well ventilated; aerial communication between it and the remainder of the house may properly be hindered by the suspension, across the doorways of the infected apartments, of sheets which are kept constantly wet with some disinfecting fluid, the wetness of the sheet being an essential point to bear in mind; sputa should be destroyed by fire or by boiling; lint, rags, and the like, used in connexion with discharges

from the throat, nose, etc., should be burned in the apartment; all china, glass, spoons, and such articles used in connexion with the patient's meals should be placed in boiling water before they are cleaned; and all communication with the remainder of the household should be avoided as far as possible. The need for stringency in these matters is often even greater during convalescence, for this is precisely the time when there is a tendency to relax them. Members of the family who are at the susceptible ages should, if practicable, be sent away from the house. On the termination of the illness all apartments and articles liable to retain infection should be disinfected.

Schools of all descriptions must always be looked upon as affording exceptional facilities for the diffusion of diphtheria. Hence, in boarding-schools, for example, all forms of sore throat should be dealt with as if infective; in the event of diphtheria being suspected, bacteriological examination should at once be resorted to, with a view to isolation both of the sick and of those in good health who are found to be harbouring diphtheria bacilli; and if, after the effectual isolation of a few first cases, the disease still shows a tendency to spread, the school should be broken up at once, and measures of cleansing and disinfection resorted to. Early bacteriological examination of material scraped from the fauces or nostrils may make it possible to take steps which will obviate the necessity of proceeding to extremes; but even in the absence of bacteriological evidence, the mere fact that "sore throat" is spreading should have great weight in forming a decision on measures of prevention. In day-schools, and notably in our elementary schools, early attacks of diphtheria have hitherto been apt to be overlooked, and until quite recently it has not been until the attendance at schools began to diminish by reason of sickness that the matter has received attention. The practice adopted in the last few years in various towns, schools, and institutions has been to isolate, as far as practicable, all persons found to be harbouring diphtheria bacilli. This involves bacteriological examination of all notified cases of diphtheria, of all cases of sore throat (attention being especially directed to such cases in school children), of all children belonging to infected families, and of all "contacts" with sufferers, particularly "school contacts." The isolation of adult healthy "carriers" may prove impracticable. "In such cases," says Dr. Cobbett, "the infectious persons should be warned that they are a danger to others, and instructed to take certain precautions. . . . In the case of children isolation will usually be practicable, and experience among the poorer classes at Cambridge has shown that they can usually be brought to assent to the removal of their children to an isolation home."

The existence of a case of diphtheria in a household in itself is a reason for excluding any member of that household from school. If, notwithstanding the exclusion of children so circumstanced, cases of diphtheria continue to manifest themselves, and if first attacks in individual households are found to occur amongst children attending particular classes in the school, it becomes necessary to close those classes; in

exceptional circumstances, where evidence of limitation of danger to particular classes is not forthcoming, a whole department, or the entire school, may have to be closed. The exclusion from school of scholars from infected houses or localities, or the actual closure of elementary schools, are matters in which sanitary authorities, acting under the advice of their health officers, are vested with considerable compulsory powers under the Education Code. It has already been shown that the reopening of schools after closure has often been the means of leading to a recrudescence of the disease, and to the development of a special potency in the infection. The recrudescences must now be regarded as mainly due to the presence of the bacillus diphtheriæ about the fauces of convalescents for a much longer period than was formerly thought at all probable. According to experiments made in the case of diphtheria convalescents, it has been found that the specific bacillus of the disease may exist in a state of vitality in swabs from the fauces, as shown by cultivation, for several weeks at least after disappearance of all local indications of any throat affection—thus a healthy child kept under observation by Dr. Graham Smith harboured diphtheria bacilli for 94 days. Bacteriological examination of such material in each individual case is necessary, and as already stated the patient should not be regarded as free from infection until three consecutive negative results have been obtained. Where such investigation is, for one or another reason, impracticable, it may be stated that in no circumstances should a child be allowed to return to school from a household in which there has been diphtheria until at least two weeks have elapsed since the last indication of throat-mischief in any one of the family concerned.

Whenever diphtheria or sore throat of an infective type is at all prevalent in schools or elsewhere, precautions should be taken to avoid the common use of drinking-cups and other like articles; kissing among children should also be avoided.

The prophylactic use of antitoxin is considered elsewhere (*vide* p. 1037).

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BACTERIOLOGY AND PATHOLOGY OF DIPHTHERIA

By the late Professor A. A. KANTHACK, M.D. Revised by F. W. ANDREWES, M.D., F.R.C.P.

There are but few infective diseases the bacteriology of which has been so completely worked out as in the case of diphtheria. Although Klebs, in 1883, had described a special bacillus observed by him in diphtheritic membranes, Löffler was the first who succeeded not only in separating it by growth in artificial media, but also in producing in animals by means of inoculations distinct lesions, said by him to resemble diphtheria. After its discoverers, the bacillus is generally called the Klebs-Löffler bacillus. Löffler's observations were soon confirmed by others, notably by Roux and Yersin in France, and Dr. Klein in England; but the final proof of the specificity of the B. diphtheriæ we owe more especially to the researches of Dr. Sidney Martin.

The Klebs-Löffler bacillus is found in every case of diphtheria; and from the results of investigations made, we may say, all over the world, we must refuse to call any lesion diphtheria, unless it is associated with that bacillus; conversely, any morbid process accompanied by this organism is diphtheria. Formerly, when physicians relied for their diagnosis merely on inspection of the affected parts, or on certain symptoms and signs, cases were excluded because they did not conform to the accepted clinical "type"; and the absence of gangrene, necrosis, or membrane was almost sufficient for a denial of the existence of diphtheria. Bacteriology has taught us that we must alter our views, and include under diphtheria many cases which, according to the older conception, would not have been called diphtheria. At the present time we frequently hear that typical bacilli have been discovered in cases which clinically are not diphtheria: our clinical notions must, then, be amended and our position reconsidered. On the other hand, but a few years ago many forms of tonsillitis and laryngitis were diagnosed as diphtheria, which now by means of an adequate examination are readily excluded. We possess, then, in this Klebs-Löffler organism a certain test, with the help of which in competent hands it is easy to decide the true nature of a suspicious case; and the vexed discussion as to the identity or non-identity of croup and diphtheria ceases henceforth. In tubercle and in

diphtheria the bacillus asserts itself with an authority which must put aside any preconceived notions.

The Diphtheria Bacillus.—This organism is extremely polymorphic, and this character greatly facilitates diagnosis. Two varieties may be conveniently described, the long and the short variety, though intermediate forms are found—(*a*) *Long forms:* These are perhaps to the beginner the most characteristic forms. They are generally clubbed at one end, and are distinctly curved or *ſ*-shaped, and frequently, when stained, have a granular or segmented appearance, as they do not take up the dye uniformly. These clubbed forms are regarded by many as degeneration or involution forms; but we shall see that this view is probably erroneous, since they are best marked in young growths. (*b*) *Short forms:* These occur, as a rule, as straight or slightly curved rods, not uniform in thickness, but generally slightly swollen at one end, or swollen in the middle with pointed ends.

It is, however, not advisable to be too strict in this division of the bacilli into types according to their size, because, although we may find growths in which all the bacilli are long and clubbed, or short and straight, they frequently vary in size and shape in the same culture, and on transferring a long form from tube to tube it often changes in appearance from the long to the short form, and conversely. It has also been stated that cases presenting the long forms are more virulent than those presenting the short form. This, however, is misleading and erroneous. After an extensive examination I can say confidently that it is futile to base a prognosis on the type of organism present. Some of the worst cases that I have seen were associated with the short variety exclusively, while many less serious cases exhibited long forms only. Again, I have found colonies of the long and the short form side by side on the same agar-agar surface.

In all cases the grouping of the diphtheria bacilli is characteristic. They never form chains or threads, but are generally arranged in irregular clusters, which in structure have been aptly compared to the irregular Chinese characters built up of lines set asymmetrically and at various angles. The bacilli possess neither spores nor flagella, and stain well with ordinary aniline dyes. Löffler's methylene blue is specially suitable as a routine stain, as it brings out well the metachromatism of the granules in the bacilli—one of their most characteristic features. By Gram's method the bacilli usually stain fairly well, though often retaining the stain less intensely than the pyogenetic cocci. Neisser's method is, however, that which gives the most distinctive results, and is to be preferred for diagnostic purposes. The film is first stained with acetic acid methylene blue, washed, and then counterstained in a contrast dye such as Bismarck brown. The granules take on an inky-blue colour, while the rest of the bacterial protoplasm is light brown. There are organisms other than the diphtheria bacillus which give a somewhat similar reaction, but the Neisser staining is a very real help in the differential diagnosis between the diphtheria bacillus and some of its nearest allies.

Artificial Cultivation.—The media best suited for artificial cultivation are serum or serum agar-agar, glycerin agar-agar, gelatin, and broth. (*a*) On the surface of gelatin the growth appears slowly, and consists at first of a series of small isolated punctiform colonies, which gradually fuse, and form a thick, opaque, uneven white or yellowish streak which is characteristic and easily recognised by those familiar with the diphtheria bacillus. The middle of the streak is thick and prominent, while at the margins the growth is thinner and expands in an irregular, uneven outline. (*b*) On the surface of agar-agar or serum the separate colonies when typical are round and whitish, with a thick, yellowish-brown raised centre. Lateral expansion as a rule is slow, but varies greatly; and in some cases the growth is entirely made up of minute dot-like colonies. (*c*) Growth in alkaline broth is rapid, the liquid becoming turbid within twenty-four hours at the body-temperature. The reaction of the culture medium at first becomes acid, but later it is once more alkaline. The development of acidity is a test of some value in discriminating between the true diphtheria bacillus and allied forms. The acidity is most clearly developed in broth containing two per cent of glucose; the reaction should be tested at the end of 48 hours, an uninoculated tube of the same medium being used as a control.

The bacilli thus artificially cultivated present the characters and grouping described above; they may appear either as long or short forms, clubbed, curved, or straight. It is in young cultures on serum or agar-agar especially that the peculiar clubbed and branched forms may be observed; so that we cannot regard these as degeneration forms, but with Dr. Klein may seek in them a clue to the ancestral history of the bacillus, inasmuch as they point to a mycelial origin. An attempt has been made to distinguish two types according to the size of the individual colonies on the surface of agar-agar; some diphtheria bacilli grow always in large colonies, and others grow always in small colonies. But this, again, is no distinctive character, since large colonies on subcultivation will frequently appear as small ones, and conversely; to a certain extent the smallness of the colonies seems to depend on the closeness and crowding together of the colonies.

Bacteriological Diagnosis.—Having shortly described the most leading characteristics of the Klebs-Löffler bacillus, it is well here to give as shortly a few directions as to the method to be pursued when a bacteriological examination has to be made for diagnostic purposes :—(*a*) If a piece of membrane is available, it should first be washed in several changes of sterile physiological salt solution; then a small piece is removed with a strong platinum loop, or the platinum needle is dug into the substance of the membrane. With the latter thus charged, a series of serum or serum agar-agar tubes are now streaked, three parallel streaks being made on each, passing from one tube to the other without recharging the needle, so that in the last tube the insemination is scantiest. The tubes are now incubated at body-temperature and examined next morning; suspicious colonies are selected, and traces thereof removed with the

platinum wire. Each colony may first be examined in the unstained condition, and if suspicious, be stained with Löffler's methylene blue or by Gram's method. Neisser's stain should always be applied as a confirmatory test, as in this way serious errors may be avoided. The diagnostic value of this stain is specially marked in young serum cultures less than twenty-four hours old. (*b*) If membrane be unobtainable, the platinum loop must be passed over or pushed into the affected part, if it be accessible, and with the charged wire tubes must be inoculated in the manner already described. This is easy enough when the fauces, nose, or conjunctiva are affected; but what is to be done in laryngeal diphtheria? Experience shows that in most of these cases the bacilli may be readily obtained from the pharyngeal or faucial—not tonsillar—secretions, and from these tubes should be prepared. In cases where material has to be sent by post for examination, it is customary to rub the fauces well with a sterilised swab of cotton wool on a wire. This is then packed in a sterile test-tube. If care be taken that the swab does not become too dry, fairly reliable results are to be obtained, but it is certainly a less trustworthy procedure than direct inoculation of the culture tubes from the throat.

For the purpose of diagnosis a medium must be chosen which, while specially favourable to the development of the Klebs-Löffler bacillus, has a retarding influence over the organisms generally associated with the latter, such as streptococci, staphylococci, and the bacterium coli commune. Cultures upon ordinary agar-agar are of little use for diagnostic purposes, as the diphtheria bacilli are overgrown by the more rapidly growing pyogenetic cocci. From practical experience I should recommend an agar-agar prepared from ascitic, pleuritic, or hydrocele fluid containing 2 per cent of a 10 per cent solution of caustic potash, with 5 per cent glycerin and 1 per cent grape sugar. It is more easily obtained and prepared than serum or serum agar-agar, since the above exudations are always within easy reach. The selective power of this medium towards the diphtheria bacillus is truly remarkable, and its inhibitory action over other organisms quite as striking. The characteristic Neisser staining is, however, less certainly manifested on this medium than on serum.

It must be remembered that membranes, produced by bacteria other than the diphtheria bacillus, may appear in the throat, and that in many cases the clinical phenomena prove to be of but little assistance; a careful bacteriological examination is therefore required. In scarlatina especially membranous sore throat is common; it may be caused by pyogenetic cocci, especially streptococci, or it may be due to the Klebs-Löffler bacillus. Hench and Heubner on clinical grounds, and others guided by bacteriological investigations, state that the scarlatinal angina appearing concurrently with scarlet fever is not true diphtheria, while the membranous inflammation following some time after scarlet fever is true diphtheria. This statement, which is also supported by Dr. Klein, is only true in a general way, and must not be taken too literally; the rule is one to which there are numerous exceptions: nevertheless it is a useful

rule, as it assists us materially in the early diagnosis of scarlet fever. Sore throats may appear in other infective fevers, and should always be subjected to a careful bacteriological examination; for in several cases of typhoid fever and measles, for instance, diphtheria bacilli have been found, and it has been stated that the palsy which occasionally appears in or after enteric fever is actually due to diphtheria intoxication.

As a rule, there is no difficulty to the experienced eye in recognising the diphtheria bacilli. Occasionally, however, there is some or even great hesitation before an opinion is hazarded. For bacilli do occur in the healthy fauces, in non-diphtheritic sore throats, and also in the nose, which closely resemble the Klebs-Löffler organism, but yet are not entitled to this name. These have been named "pseudo-diphtheria bacilli." The name *pseudo-diphtheria bacillus* apparently includes several varieties and species, and must be used with caution. At present there are at least two views and over half a dozen different descriptions of the alleged pseudo-diphtheria bacillus. Some observers give this name to organisms which bear a superficial resemblance to Löffler's bacillus, but which any critical bacteriologist would not and could not confound with it; others use the term for organisms which morphologically cannot be distinguished from the typical diphtheria bacillus, but which differ from it in so far as they fail to evince any pathogenetic properties when tested on guinea-pigs. This is not the place for the discussion of this question, but I think that we may fairly deny the claim of the former group to the title pseudo-diphtheria bacillus, just as we deny the claim of the bacillus coli communis to pose as a pseudo-typhoid bacillus. Whether, however, the virulence test is satisfactory and exclusive is a doubtful matter: on the face of it, it seems a weak reed to rest upon, and until stronger evidence is forthcoming, it is safer to regard with great suspicion any bacillus which not merely resembles the diphtheria bacillus, but agrees with it in every point except that of virulence; and this the more since Roux and Yersin have asserted that on one and the same agar-agar or serum surface we may find virulent and non-virulent forms side by side, and also since it is easy to deprive the true bacillus of its virulence. The French writers, in fact, consider that the so-called pseudo-diphtheria bacillus is a form of the true Klebs-Löffler bacillus, the virulence of which has become attenuated. In addition to this attenuated form of the true diphtheria bacillus, there is a species known as Hoffmann's bacillus, common in the healthy nose and throat, which may readily be confounded with the Klebs-Löffler organism. Morphologically it is scarcely distinguishable from it, but is not pathogenetic, forms alkali instead of acid in glucose broth, and scarcely reacts to the Neisser stain in young cultures. If the term "pseudo-diphtheria bacillus" is to be retained it is to this organism that it is most justly to be applied. The xerosis bacillus, common in the conjunctiva, is too small to be easily confused with B. diphtheriæ: it forms no acid in glucose broth. Dr. Gordon has recently discussed the differentiation of these diphtheroid organisms. He has also pointed out that, in serum cultures, certain streptococci, and notably the streptococcus which Dr. Klein

has associated with scarlet fever, may exhibit bacillary forms which may closely mimic the diphtheria bacillus. Attempts have been made to differentiate these various diphtheroid organisms by agglutination experiments with the serum of immunised animals. Such partial success as has been obtained is in favour of the view that Hoffmann's bacillus is specifically distinct from the Klebs-Löffler organism.

Pathogenetic Properties.—We must now briefly consider the evidence on which the specific relation between diphtheritic processes and the Klebs-Löffler bacillus has been established. (1) If we except the cat, spontaneous diphtheria is not found in animals; the diphtheria-like lesions occurring in them are due to organisms other than the Klebs-Löffler bacillus (cf. p. 977). In the cat, however, a disease characterised by bronchopneumonia, kidney disorder, and ophthalmia is described: in the consolidated areas of the lung Dr. Klein discovered the diphtheria bacillus in considerable numbers; and on artificial inoculation local diphtheritic changes were produced. Hence Dr. Klein concludes that cats are susceptible to human diphtheria, and that in them a disease occurs, centred chiefly in the lungs, which is akin to the affection in man. Those who are acquainted with Dr. Klein's researches in this matter can hardly question the truth of his conclusions; and since we are gradually recognising that the diphtheria bacillus is capable of producing non-membranous lesions, and that, when it finds access to the lungs, it may lead to pronounced bronchopneumonia, they gain considerably in significance. However this may be, inoculation of the conjunctiva or of the buccal mucous membrane of the cat with diphtheritic material is followed by changes closely resembling human diphtheria. Löffler, Welch, and others succeeded in producing membranous inflammation in guinea-pigs by vigorously inoculating the vaginal mucosa; and in rabbits by treating the conjunctiva or tracheal mucous membrane in a similar manner. In some instances paralysis followed the inoculation.

Subcutaneous injection of virulent diphtheria bacilli, whether of fresh broth cultures or of gelatin cultures suspended in broth, leads to death of the guinea-pigs in from eighteen to seventy-two hours. The first changes to be noticed are swelling at the seat of inoculation—due to round-cell infiltration, œdema, and exudation; also, as a rule, considerable local necrosis, and degenerative changes of the heart and the voluntary muscles. From the seat of inoculation diphtheria bacilli can easily be recovered, and occasionally also from the blood and from more distant organs, as, for instance, the lymphatic glands, spleen, and liver. The guinea-pig, being highly susceptible, is the animal generally used for these experiments: if it be inoculated in a hind extremity with a small quantity of virulent material there appears first a distinct fibrinous exudation, surrounded by more or less extensive hæmorrhagic œdema; the lymphatic glands in the neighbourhood soon swell; the exudation becomes more marked, necrotic changes take place, and the animal gradually wastes and dies, showing, besides the local lesions, hæmorrhagic redness of the suprarenal capsules, pleural exudation, and degenerative changes in the muscles

and nerves. Occasionally death is delayed even in these highly susceptible animals, and then paresis or even complete paralysis of the extremities shows itself, and the nerves show advanced degeneration.

(2) The most striking morbid phenomenon in the course of human diphtheria is the loss of muscular power which accompanies or follows the acute disease. When it was shown that even these characteristic symptoms could be reproduced in the animal by artificial infection, doubt as to the specific action of the Klebs-Löffler bacillus could scarcely persist any longer. Roux and Yersin demonstrated that the inoculation of the poisonous products precipitated from broth cultures is followed by paresis, a point which has received general confirmation. Dr. S. Martin has elaborated this question still further, and has demonstrated, so far as it is possible, the chemical and physiological identity between the toxins produced in artificial growths and the toxins produced in the human body. Their inoculation into the animal is followed by the same results, namely, by paresis, primary nerve-degeneration, fatty degeneration of the cardiac and skeletal muscles, and respiratory disorder. The agreement in almost all points is so close that none but those who refuse to accept the conclusions obtained through animal experiments will deny that in the Klebs-Löffler bacillus we have the specific cause of diphtheria.

(3) The last vestige of doubt must be removed by the triumphant results of treatment with antitoxin. The serum of an animal protected against the diphtheria bacillus cures diphtheria in man. As this action is specific, it follows that the animal which gave the serum was protected against an infection equivalent to diphtheria; that is, that the Klebs-Löffler bacillus is the immediate cause of diphtheria.

The Pathology of Diphtheritic Infection.—It may be said, with some degree of truth, that the diphtheria bacillus is found only in the affected area and its neighbourhood; so that the chief symptoms of the disease are due to intoxication by the poisons locally manufactured at the seat of infection. Until recently, and especially in this country, this was accepted almost as a law; recent researches, however, show that we must modify our views somewhat, for it has been demonstrated that after death the bacilli may be traced in certain viscera and organs not in direct communication with the diseased tissues. In the membranes, or at the primary seat of infection, they occur in largest numbers, and here the toxin is most copious; in distant parts the organisms, when present, are generally scanty and the poison more diluted. Hence, with due reservations, the original statement may be allowed to stand, and we may look to the seat of infection as the source of all the trouble. At the same time we must keep in mind that the bacilli may escape, and do escape oftener than is generally imagined, into the blood or more distant organs; this is true especially of those cases which end fatally, and on them most of our pathological observations are based. This question, which here can only be considered in all brevity, has been more fully discussed by myself [A. A. K.] and Dr. J. W. W. Stephens. The bacilli may escape from the seat of infection along various paths:

(*a*) by transference of the *contagion* to other parts of the body, as, for instance, cutaneous infections during the course of diphtheria; (*b*) by direct extension of the diphtheritic process (with or without membranes) along the open passages in communication with the seat of infection, that is, for example, from the tonsils or larynx upwards to the nose, eyes, and ear, and downwards to the trachea, bronchi, bronchioles, and lung alveoli, œsophagus, stomach, and intestines; (*c*) by extension along the lymphatic channels into the cervical, submaxillary, or bronchial glands; (*d*) through the circulation into the spleen, liver, kidney. Now it is evident that the first and second conditions cannot influence the generally accepted notion of a local infection, for in the one case we have an accidental additional lesion, and in the other merely an increased area of infection by continuity; but the other two conditions, if they occur frequently, would compel us to change our views. At present we do not possess sufficient information as to how often distant glands and distant organs contain diphtheria bacilli; but from the observations of others and ourselves, it is certain that in the spleen, for instance, they may be found, at any rate in fatal cases, comparatively often. Thus Frosch, Kolisko, and Paltauf and Booker, Wright, and Stokes collectively discovered them there fairly often, and in twelve consecutive post-mortem examinations we obtained positive results in nine cases; hence it can no longer be doubted that an escape into the circulation does occur in lethal cases, and especially when a tracheotomy has been performed. Nevertheless for the present and in a general way we may regard diphtheria as primarily a local infection, the bacilli being found in enormous numbers at the seat of lesion, whence the deadly poison or poisons secreted or manufactured by them pass into the system.

To the pathologist, then, the toxic substances are of the utmost importance, and to them we must now turn our attention. Roux and Yersin first demonstrated that by injection of the toxic products of the diphtheria bacilli into susceptible animals the nervous lesions so characteristic of the human disease may readily be induced in such animals. This observation was followed up and confirmed by Brieger and Fränkel, and more especially by Dr. Sidney Martin in this country. Roux and Yersin obtained the toxin by precipitation with alcohol and phosphate of lime, and therefore inclined to the belief that this substance is a ferment, or, more correctly speaking, an enzyme; while Brieger and Fränkel saw in it a toxalbumin, or rather a mixture of toxalbumins. Dr. Martin's experiments were more thorough than those of his predecessors. He separated from the blood, spleen, and other viscera of children dead of diphtheria, albumoses (chiefly deutero-albumose) and an organic acid; the former being always present in far greater quantity than the acid. Subcutaneously injected into guinea-pigs, the albumoses produced local œdema and slight irregularity of the body-temperature. When, however, they were intravenously injected into rabbits, the result was fever, or a lowering of the temperature, loss of coagulability of the blood, paralysis of the hind legs, coma, and death. Oft-repeated intravenous

injections of small doses were followed by fever (variable in degree), paresis (a constant effect), respiratory disturbances, loss of weight, and diarrhœa. The fever may last a long time, the paresis may appear suddenly and rapidly, but its progress is slow, and the loss of weight is always tardy. The paresis is best seen in the extremities, but affects also the trunk muscles. There is no visible atrophy of the muscles and no loss of the knee-jerk. On examining the animals after death bacilli were not found, so that the lesions were due to the chemical substances; that is to say, were truly intoxicative. The organic acid, like the albumoses, is a nerve poison, but not nearly so toxic. From diphtheritic membranes fibrin, hetero-albumose, traces of proto- and deutero-albumoses and of organic acid were obtained; but the membrane extract consisted of proteid substances with minute traces of albumoses, which extracts, when administered to rabbits, produced fever, paresis, and death. It is thus seen that the membranes contain proteid substances which are not albumoses, but have, nevertheless, the same action; they are, however, far more virulent than the albumoses. From pure cultures of the Klebs-Löffler bacillus the same albumoses and organic acid were obtained, and these displayed the same physiological action as the tissue-substances. Dr. Martin concludes that the bacillus diphtheriæ produces the same substances in the culture media as in the tissues, that these have the same action when injected into an animal's body, and that undoubtedly the bacillus of Klebs-Löffler is the immediate cause of diphtheria. Since the membrane extract contains no albumoses worth mentioning, and yet is extremely toxic, it is possible that in them a ferment-like substance is formed which, absorbed by the tissues, splits them up by virtue of its digestive action into toxic albumoses and an organic acid; and that the albumoses thus manufactured will produce the characteristic lesions in the animal organism.

This ferment-like body or enzyme corresponds to that obtained by Roux and Yersin, and is formed in and secreted by the bacilli themselves. Dr. Martin explains the pathological process in this manner. Since the infection is primarily a local one, the organism at the primary seat of lesion secretes a potent proteolytic enzyme which enters the tissues and blood, and wherever it comes in contact with them, digests them; the products of this digestion are toxic albumoses and the organic acid, substances which are diffusible and, on being absorbed, lead to the morbid changes and disturbances which belong to the diphtheritic infection. This view, tempting though it may seem, cannot be accepted in the form in which Dr. Martin offers it; Dr. Martin has not taken into consideration that in fatal cases of diphtheria the bacilli are frequently found in the lungs, spleen, and other organs; and therefore it seems far more probable that the toxin is secreted directly by the bacilli than produced by intermediary fermentative processes. The spleen contains toxins because they have been absorbed, and often for the further reason that bacilli have found their way there; and since the bacilli are vastly more numerous in the membrane than in the spleen, we

find a poison of lesser virulence in the spleen. The albumoses may be merely contaminations which happen to come down with the reagents which precipitate the true toxin; the latter is a direct cellular product of the organisms—according to Gamaleia a nucleo-albumin—which is absorbed by the tissues, blood, and lymph. There is no evidence that the process of intoxication is an indirect one, the bacterial cell forming an enzyme, the enzyme producing albumoses, and the latter inducing the intoxication; on the contrary, we may assume that the bacterial cell secretes its toxin, whatever its nature may be, and that the latter is observed as a direct tissue poison.

Whatever view we take of the nature of the poison or of the process of intoxication, the laboratory has conclusively demonstrated that the Klebs-Löffler bacillus is the cause—the specific cause of diphtheria: whether we inoculate the animal with the living germs or with the toxic products, all the characteristic symptoms and lesions of diphtheria can easily be reproduced by carefully thought-out experiments.

There is, however, another point to be considered briefly, namely, "mixed infection." But rarely on examining diphtheritic membranes do we find pure growths of Löffler's bacillus; as a rule the latter is associated with various streptococci and staphylococci, many of which belong to the group of pyococci. Is their presence of significance? Dr. Martin, foreign observers, especially Roux, and others assert that such an association is most unfavourable, while Drs. Washbourn, Goodall, and Card do not consider the association with streptococci on a single bacteriological examination as evidence of unfavourable import; in fact, they incline rather to the opposite conclusion. Personal observation made at St. Bartholomew's Hospital, where as a rule only serious cases are admitted, leads me to believe that the presence of streptococci in itself does not influence the prognosis; indeed that, as a matter of fact, they are rarely found absent, whether the cases be mild or serious, if a series of cultivations (two or three tubes) be made in every case. When we consider that streptococci are the most abundant organisms in the normal mouth-secretions, numbering many millions per cubic centimetre, it would be a matter for some surprise if they were not usually present in cultures from diphtheritic sore throats. There can be no doubt, however, that secondary septic complications, such as suppurating glands, suppurative otitis media, septicæmia, and pyæmia may be produced by these organisms. Most so-called septic and hæmorrhagic forms of diphtheria are caused by secondary pyococcal infection. It is, however, a mistake to consider all swollen and inflamed glands, and all forms of lung affections such as bronchopneumonia or otitis media, as being exclusively caused by these pyogenetic organisms. In the cervical and bronchial glands the Klebs-Löffler bacillus is frequently found; so it is also in the lungs after death, and occasionally in the middle ear. Nevertheless it is of the utmost importance to keep in mind the possibility of a secondary infection, since, when we come to treatment, we cannot expect a serum which specifically counteracts the diphtheritic process to be potent also against the pyococcal infections. For this reason

the employment of an antistreptococcal serum has been suggested, and in France this plan has been adopted (*vide* p. 1035). Hæmorrhagic diphtheria seems to be generally due to secondary infection, for in two or three cases examined personally, or in conjunction with Dr. J. W. W. Stephens, I [A. A. K.] found pyococci (pneumococci and streptococci) in the blood and organs; in a third case, however, the diphtheria bacillus existed in the spleen. The mortality of this kind of diphtheria is always high, in spite of the antitoxin now used; and we can readily explain the failure of this remedy if most forms of hæmorrhagic diphtheria are due to secondary infection or are true septicæmia. Bronchopneumonia has also been generally attributed to streptococci; but my own observations and those of Wright, Frosch, Stephens, and others tend to prove that in most cases we have a true diphtheritic infection in the lungs; and in almost all fatal cases, especially if the process were laryngeal, or if tracheotomy had been performed, the Klebs-Löffler bacillus can be found in the lung. This point is worthy of the fullest consideration, since it shows the necessity of active and energetic antitoxin treatment in such cases; in these the area of toxin-production must be enormous, and, as the lungs are extremely vascular, absorption thence must indeed be great.

Although I feel tempted to say a few words on cutaneous and ophthalmic diphtheria, in order not to extend this article too much, I must now pass on to the morbid anatomy of diphtheritic processes.

Morbid Anatomy of Diphtheria. — (*a*) Membrane: The presence of true or false membranes was formerly considered the characteristic of diphtheria, but, as we have already seen, it is by no means essential. If, for instance, we regard the process as it occurs in the tonsils and fauces, we may have extensive membranes, or small patches or mere powdery flakes; or again we may find an entire absence of membranous exudation. There may be mere redness or œdematous swelling, or there may be a gangrenous or necrotic lesion. Yet since the membrane must, for the present at least, remain an important clinical diagnostic factor, a few lines must be devoted to its description. These membranes consist mainly of fibrin, and are either coherent patches or small whitish flocculi; they may be firmly or loosely adherent. In most cases the surface epithelium is shed in part before the deposition of fibrin begins; but membranes may also appear in, over, and even under the intact epithelium. When fully formed they consist of filaments of fibrin, which form a network enclosing within its meshes leucocytes, red corpuscles, and bacteria. The thickness and size of the fibrin filaments vary considerably, and, if the membranes are firm, lamination is often seen. When detached they leave a reddened surface behind which, as for instance occasionally on the tonsils, may be in a state of ulceration; a second membrane may quickly develop on the denuded surface. Formerly distinctions were drawn between diphtheritic and croupous membranes—true and false membranes: there is, however, no reason why we should adhere to this more or less artificial division. Dr. Klein (16) summarises the more recent views tersely, and his words may be quoted with advantage:—

"True diphtheritic change of mucous membrane is regarded as involving exudation into the mucosa itself—a condition resulting, under engorgement and stasis in the vessels of the mucosa, in complete necrosis of that tissue. In this latter circumstance the mucosa becomes in effect diphtheritic membrane; its superficial part contains leucocytes, its middle or main part is a reticulated fibrinous necrosed tissue, while its deeper part, that in contact with the inflamed but still living portion of the mucous membrane, contains, like this latter, leucocytes. Most text-books now represent the above anatomical conditions as differentiating croupous and diphtheritic change of mucous membrane."

So far as diphtheria is concerned, we have first, when membranes appear, a superficial exudation into the epithelial surface, with fibrin-formation and degeneration of the epithelium itself. Now the necrosed epithelium gradually disappears, in part or entirely; and the underlying connective tissue or tonsillar tissue becomes covered by a fibrinous layer containing dead epithelial cells, leucocytes, and the like, which gradually extends into the deeper strata of the mucous membrane or tonsil. Fresh layers of fibrin may be added until perhaps a thick membrane is formed. In the superficial layers, which generally are the oldest, cocci may be found; while in the deeper and younger layers we often find the diphtheria bacilli unmixed with other organisms. Often enough, however, the diphtheria bacilli are found in any part of the membrane. The tissue below the membrane is in a state of inflammation, showing collections of leucocytes, or fibrinous exudation and hæmorrhages, and, according to my own observations, may be invaded by the bacilli. Healing as a rule takes place without scarring, unless the tissue-defect were so serious as to lead to destruction of the mucosa. It is interesting to remark that the diphtheria bacilli, even in fatal cases, are frequently found in the leucocytes, which may be almost over-distended by the engulfed organisms. With the disappearance of the membrane the bacilli also generally disappear. In many cases, by means of careful test-tube experiments as the cases progress towards recovery, a steady diminution in the number of the specific organisms can be demonstrated. Exceptions to this rule, however, are numerous, for even after apparent recovery the bacilli may linger in the throat not only for weeks, but in rare cases for many months. In such cases they may be impaired in virulence, in others there is no attenuation. These observations show the necessity of examining the throats of patients who have been treated in hospitals before dismissing them; such patients must not be discharged until the bacilli have completely disappeared, since otherwise they may become sources of infection.

Membranes may be seen in the mucous membrane of the soft palate and its pillars, the tonsil, fauces, and pharynx, and the larynx; and may extend also into, or appear primarily in the nose, conjunctivæ, trachea, and bronchi; more rarely they extend into the œsophagus, or appear in the stomach and intestines. In cutaneous diphtheria membranes also generally cover the sores. When the process extends into the bronchi a diphtheritic bronchopneumonia follows as a rule; and we often observe

in the alveoli a fibrinous network enclosing the bacilli: as I have said, there can be no doubt that diphtheritic bronchopneumonia or capillary bronchitis is much commoner than is generally believed. A curious and important pathological condition is the so-called rhinitis fibrinosa, where we find membranous casts on the nasal mucosa. Clinically such cases are not diphtheria, but pathologically and bacteriologically they are so; in the cases I personally examined I obtained, as others did, large numbers of virulent diphtheria bacilli. These chronic fibrinous inflammations constitute what might be called "chronic diphtheria,"—not dangerous, perhaps, to the individual, but deserving the fullest attention as a source of infection.

Besides the local changes in the parts mentioned, morbid appearances may be found (*a*) in the lymphatic glands, (*b*) the spleen, (*c*) kidneys, (*d*) heart, and (*e*) in the nervous system. The glands, especially the cervical or bronchial, according to the seat of affection, are swollen, inflamed, or even in a suppurative condition. The spleen is frequently enlarged and injected or congested, though rarely soft; the kidneys are generally pale and cloudy, and microscopically they may show evidence of epithelial necrosis, fatty degeneration, or even of actual nephritis. The muscular tissue of the heart may be in a condition of fatty degeneration, which varies to a greater or less degree, but is frequently absent. Of greatest interest are the nervous changes, which have been more carefully studied by Déjerine, Gombault, Meyer, and Dr. Sidney Martin. The paralysis following diphtheria is due to a parenchymatous degeneration in the peripheral nerves; so that the expression "peripheral neuritis," as commonly understood, is in this connexion misleading. The white substance of the medullated fibres is broken up and attenuated, or may disappear altogether; the primitive sheath remains intact, and the axis-cylinders are frequently ruptured. The nerve-fibres below the rupture then undergo the Wallerian degeneration, the white substance breaking up along the whole course of the fibre, and the axis-cylinder also degenerating. The different branches of the same nerve are affected to a varying degree, so that there are generally some fibres intact which can still innervate the muscle if a motor nerve be affected. This explains why during life the paralysis is as a rule partial and not complete.

The sensory and motor nerves may suffer alike, and so may also the sympathetic nerves; except that in the latter case we find changes only in the axis-cylinders, there being no visible medulla. Some observers have described changes in the cells of the anterior cornu of the spinal cord, or have ascribed the nervous changes to a mild form of poliomyelitis. Dr. Martin, in the observation from which I have amply quoted, considers them all to be essentially peripheral, and has never detected lesions in the ganglia or central nervous system. This matter is still under discussion, and cannot be considered as finally settled. Meyer has described an increase of nuclei of the nerve-fibres, and also nodular swellings of the nerves formed of cellular elements; but according to Dr.

Martin these changes probably only indicate an attempt at repair of the nerve.

The distribution of the nervous lesions will be considered in the clinical portion of this article, and I may conclude by mentioning that, necessarily, the muscles supplied by the diseased nerves are also degenerated to a degree proportional to the nerve-lesion. The muscular fibres may present advanced fatty degeneration to such an extent that all fibres are affected; or fatty fibres may be mixed with normal ones, or parts of a fibre only may be fatty. It seems that the diphtheria poisons are special nerve poisons, for Dr. Martin has shown in man that even during the course of an acute attack which lasted only five days nerve-degenerations may appear.

The same observer further states that fatty degeneration of the cardiac muscle is observed chiefly in fatal cases of diphtheritic palsy or in cases which die in syncope; hence the signs of cardiac failure in diphtheria are due to a direct influence of the diphtheria toxins on the cardiac muscle: this is the more probable as the heart of the experimental animal is easily affected by these poisons.

In discussing the pathology of diphtheria I cannot conclude without saying a few words on the hæmic changes, that is, on the increase or decrease of the number of leucocytes and on the possible import of these conditions. Most writers are agreed that diphtheria is accompanied by a marked leucocytosis, which increases as the disease progresses, and again diminishes during convalescence, disappearing soon after the membrane. This leucocytosis is of the ordinary febrile type, affecting chiefly the polymorphonuclear, neutrophil (finely granular oxyphil) corpuscles. Gabritschewsky states that this increase in the number of leucocytes is greatest in fatal cases, and believes that a progressive leucocytosis implies a bad prognosis. After antitoxin injections the leucocytosis steadily diminishes as it does in convalescence, and the hæmocytometer is, therefore, according to him, a useful means of gauging the success of treatment. Dr. Ewing does not consider the high leucocytosis to be necessarily an unfavourable sign, for it may mean merely a pronounced reaction, but he agrees with others that in fatal cases there is leucocytosis till death; in mild cases the leucocytosis is but slight, and the leucocytosis steadily decreases in favourable cases. Dr. Morse, on the other hand, does not think that the examination of the blood is of value in prognosis, because, although fatal cases generally have a well-marked leucocytosis, it is not always present, and even in the mildest cases is often very pronounced. Judging from personal observations made at St. Bartholomew's Hospital in conjunction with Mr. E. L. Lloyd, I agree with this writer on the prognostic value of the leucocytosis in diphtheria. The daily counts made in a series of cases show that—(1) broadly speaking, a high leucocytosis signifies a good reaction, and was present in those which recovered; (2) a low leucocytosis at the height of the disease, before antitoxin has been injected, accompanies most, if not all the fatal cases; (3) the high leucocytosis of well-reacting cases, after and during antitoxin treatment, steadily diminishes, the number of cells decreasing by 50 per

cent in three to four days. Dr. Waldstein states that when during convalescence the leucocytosis declines, the number of "neutrophil" cells falls rapidly, while the mononuclear or lymphocytic elements increase; in the lymphocytosis he sees a prognostic sign of great value, so much so that he recommends subcutaneous injections of pilocarpine, in order to raise artificially the number and ratio of the lymphocytes.

Artificial Immunity.—Guinea-pigs, which are highly susceptible animals, can be protected against an infection with the Klebs-Löffler bacillus in various ways: (1) by means of subcutaneous injections of broth cultures sterilised by heat or attenuated by adding trichloride of iodine; (2) by means of prophylactic injections of hydrogen peroxide; (3) by a successful cure of an experimental infection; (4) by means of Behring's combined method, which consists in the administration first of attenuated cultures, followed by that of fully virulent ones or of strong toxin; (5) by means of feeding with diphtheria toxin. The serum of a highly protected animal, when injected into a guinea-pig in a normal state, possesses the remarkable property of rendering it immune; and, when injected into one already suffering from the effects of a diphtheritic lesion, of curing it. This gives us the 6th method of artificial protection, namely, the injection of protective serum or antitoxin, and on it is founded the serum treatment of diphtheria to be discussed presently. To obtain a good and active serum horses may be injected with toxins, gradually increasing in dose and virulence, or with the bacteria themselves, beginning with their dead bodies and gradually proceeding to large doses of living bacilli; or these two methods may be combined in order to obtain a serum which is both strongly antitoxic and highly protective. The immunity which this serum is capable of conferring on animals is of comparatively short duration (one to two weeks, and at most ten weeks); and when used on man is so slight as to be of little value for prophylactic purposes. Thus in a case under my own observation, a child acquired true diphtheria within two weeks after a copious administration of the antitoxin, which had been given for an angina erroneously diagnosed as diphtheria. Its curative value, however, as we shall see, cannot be questioned.

A word may be added in conclusion as to the terms used in measuring the strength of the diphtheria toxin and antitoxin. Neither has been brought within the ken of ordinary chemistry: they are at present recognised only by their physiological effects. But Ehrlich has pointed out that the diphtheria toxin is so uniform in its action upon the guinea-pig that this animal may be employed as an index for measuring its amount, thus bringing the matter within the range of reasonably accurate numerical expression. The "*toxic unit*" now almost universally employed is that introduced by Behring. It is the amount of toxin which just suffices to kill, in four days, 100 guinea-pigs weighing 250 grammes apiece—*i.e.* the minimum lethal dose for 25 kilogrammes of guinea-pigs. The corresponding "*antitoxic unit*," in terms of which the dosage of commercial antitoxin is always stated, is the amount of antitoxin which will just neutralise the toxic unit, *i.e.* which will just save 25 kilogrammes of guinea-pigs from

the minimum lethal dose of toxin, the two being mixed and injected together.

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CLINICAL FEATURES

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Order of Development of Diphtheria.—The first result of diphtheritic infection is local. The infected part inflames, and it is in and upon the inflamed tissues that the morbific microbes increase and multiply. Infection of deeper organs and of the whole body is chiefly due to absorption of soluble venom from the place where the growth of microbes is proceeding. Thus diphtheria may be compared with syphilis: the primary pellicular inflammation of the one and the primary sore of the other being strictly analogous; from the primary lesion the secondary infection of the whole body proceeds in both cases. This close analogy was discerned by Bretonneau (4), and the most recent and complete experiments upon lower animals have confirmed the accuracy of his opinion.

Omitting for the moment consideration of the nasal passages, the primary seat of infection is seldom any other than the fauces or larynx. Hence two chief forms of diphtheria. The symptoms and whole appearance of the disease differ so much according to the part first affected, that many years elapsed before physicians universally accepted Bretonneau's

doctrine of the essential identity of faucial diphtheria and membranous croup.[1]

Simple and Malignant Diphtheria.—From the time of Aretæus a distinction has been made between mild (or simple) and pestilential (or malignant) diphtheria. Simple diphtheria is that which is characterised chiefly by the local affection; malignant is that in which toxæmia predominates: the blood, and through it the whole body, being poisoned by venom prepared at the primary local lesion.

A. Diphtheritic Sore Throat (Angina faucium)

In the following pages diphtheria will be described analytically, symptom by symptom, yet not without reference to the association and succession of symptoms. A general description of the disease must always be more or less imaginary, and can never tally with actual experience and matter of fact—so many are the symptoms of diphtheria, and so infinitely varied is the manner in which they are associated.[2]

I. Prodroma.—The first symptoms of disease relate either to the fauces or to infection of the blood; the diphtheria is manifested first in the throat or not. Symptoms which are due to infection of the blood, and precede any sensible affection of the fauces, are called prodroma or premonitory symptoms.

i. *Fever*, which is probably an early symptom in all cases, in some is the very earliest, preceding any signs of local disease. The onset is sometimes gradual and insidious, sometimes sudden and marked by chilliness, not enough to cause shivering. The temperature seldom rises above 103° F. Premonitory fever is of uncertain duration, seldom lasting more than a day or two.

ii. Fever will be accompanied by its usual concomitants—drowsiness, giddiness, peevishness, aching and pains in the limbs and back; the frequency of the pulse will be increased, the digestion disordered. The digestive disorder, indicated by vomiting, disgust for food, headache, weariness and low spirits, will sometimes last fully four days before the sore throat begins, and may be (perhaps with reason) attributed to "biliousness."

iii. *Spontaneous lassitude* is, in some patients, the most marked premonitory symptom—a great sense of weakness and weariness, lasting about four-and-twenty hours before the throat becomes sore. When the

[1] "You have not forgotten the celebrated *Concours*, ordered by the Emperor (Napoleon I.) at the death of the young prince, his nephew, nor the division of the great prize between Jurine of Geneva and Albers of Bremen, authors of Memoirs, in which they both declare that angina maligna is a distinct and opposite disease from croup. No matter!"—(3) p. 179.

[2] "Some such descriptions, when they have conveyed the truth with great force and faithfulness, have been regarded with the same sort of pleasure with which we look upon a well-drawn picture. But, after all, they are more pleasing than profitable. Perfection in this kind was reached ages ago, yet we go on describing what has been better described before, and are venturing with rash hands still to retouch the masterpieces of Aretæus."—P. M. Latham, *Dis. of Heart*, vol. i. p. 106.

lassitude exists, as it may, nearly a week before the onset of sore throat, it lies open to question whether the lassitude is to be attributed to the diphtheria or to some other form of blood-poisoning (such as biliousness); whether, in other words, the specific invasion (or prodromal) period of diphtheria can last so long.

II. The Sore Throat.—In most cases the disease is first manifested in the throat or neighbouring parts, and by one or more of the following symptoms:—

i. Soreness of the throat, especially felt on swallowing, and sometimes causing cough. In young children the sore throat is indicated by disinclination to swallow. But the soreness is sometimes very slight, and may not be complained of even when examination shows that false membranes have already formed upon the fauces.

ii. Noise in breathing, snoring, breathing with mouth open, change in quality of voice—all due to swelling of fauces.

iii. Coryza, sneezing, nose-bleeding—due to simultaneous affection of nasal fossæ.

iv. Swelling of neck on one side or on both; enlargement of lymphatic glands at angles of lower jaw; pain felt in neck, especially on movement.

v. Visible appearances in the throat; these demand much more close attention: they are of four kinds, appearance before occurrence of false membrane, false membrane, swelling, and muco-purulent secretion.

1. *Inflamed Throat before Formation of False Membrane.*—When an opportunity is afforded for examining the fauces before the appearance of false membrane, they are seen to be swollen, sometimes pale and glistening, or sometimes reddish. There are no signs by which the naked eye can distinguish diphtheritic inflammation (before the appearance of false membrane) from other kinds of inflammation. Upon this inflamed surface false membrane appears sooner or later. In some cases it is formed very rapidly, for however soon the throat be examined after the first signs of local disease, false membrane is seen. On the other hand, several days may elapse before the angina becomes pellicular.

The diphtheritic affection of the throat does not always result in formation of false membrane, and this non-pellicular angina constitutes one form of latent diphtheria.

2. *False Membranes.*—The first appearance of false membrane is as one or several small whitish specks or patches. Although there is no part of the throat where they may not first appear, they are especially apt to begin upon the tonsil or uvula. The margins of the mouths of the tonsillar crypts are often first affected, a point which will be alluded to hereafter with reference to the diagnosis of false membranes which are diphtheritic from those which are not. The diphtheritic membrane differs much in different cases in respect of—

(*a*) Texture; being firm, tough, and coherent, or soft, loose, and friable.

(*b*) Thickness; at first, being thin, the membrane is transparent, opaline, afterwards quite opaque.

(*c*) Extent; by which the activity of the disease, so far as the throat alone is concerned, is to be judged of chiefly. But at first it cannot be said what the final extent of membrane may be; a very small pellicle may be the beginning of very extensive disease. Rapid extension is a sign of virulence: in forty-eight hours from the beginning of exudation the whole soft palate, uvula, tonsils, and pharynx may be invaded, not to speak of the posterior nares, root of tongue, larynx, and even other parts of less importance, to be named hereafter as occasional seats of diphtheritic disease.

(*d*) Adhesion to the tissues beneath, that is to say, to the mucosa; the membrane is sometimes very adherent, sometimes it can be removed by a soft brush with ease. The mucosa is left very slightly abraded and looking almost natural, or it is swollen, ragged, and bleeding. A new false membrane is formed upon the raw surface, and sometimes very rapidly, within two or three hours.

(*e*) Decomposition of the false membrane sometimes occurs, and indicates a bad form of disease. The whitish colour is lost and the membrane tends to become blackish; the smell of the breath is most offensive: putrid sore throat.

These differences in the false membrane are mainly due to differences in the relative abundance or activity of the several microbes growing in the exudation—whether specific bacilli, divers pyogenetic micrococci, or common putrefactive microbes. When the specific bacillus is the prevailing microbe, the false membrane is tough, coherent, and not prone to decomposition; the puriform discharge from the affected part is scanty; when the false membrane is carefully removed, the mucosa beneath seems not to be much affected and does not bleed. When streptococci are found alone, or are largely mingled with the bacilli, the exudation is softer, more pulpy, more prone to decomposition and to be attended by an abundant puriform discharge; removal of the false membrane exposes a swollen, raw, and bleeding mucosa.

3. *Swelling of parts beneath false membrane* is usually proportionate to the activity of the local disease. Swelling of the fauces sometimes becomes so great in two or three days that the uvula is pushed back and invisible, even the tonsils cannot be distinguished, and the isthmus faucium is reduced to a narrow vertical slit in the middle line. In consequence of this inflammatory swelling, the soft palate may be not less than three-quarters of an inch thick, firm and tough.

4. *Muco-purulent Secretion.*—Abundant puriform discharge from the fauces occurs in severe cases so as to interfere greatly with examination. The secretion is sometimes offensive to smell. If a similar discharge (watery at first, afterwards more purulent) occur from the nostrils or ears, it may be assumed that the nasal fossæ or tympana are invaded, and the disease is so much the more serious, because more extensive. The discharge from the nostril is acrid, and excoriates the upper lip in a manner quite comparable to the effect of the vesicating virus of cantharides, as Bretonneau pointed out. No doubt this diphtheritic fluid is also a

powerful irritant to the mucous membranes with which it comes into contact, and thus prepares the way for the growth of false membrane. Cutaneous erysipelas sometimes starts from the point where these irritating discharges reach the surface of the body—a complication especially apt to occur in diphtheritic otorrhœa.

5. *False Membrane cast off.*—After the false membrane has ceased to grow it is soon cast off, either as coherent flakes or shreds, or soft pulpy material. The mucosa beneath is left at first somewhat reddened and perhaps swollen. Mere excessive redness soon passes away, swelling less quickly.

Ulceration of the mucosa will follow but seldom upon the false membrane being thrown off. The ulcers may be deep, and on both sides of the throat, quite like the ulcers of scarlatina anginosa; the tonsil will sometimes be destroyed so as to leave a ragged cavity; the soft palate and uvula may be extensively ulcerated or sloughy; the mucous membrane about the epiglottis and aryepiglottic folds may suffer in like manner.

6. *Relapse.*—After the false membrane has been cast off, but before the patient has recovered from the whole disease, a renewed exudation upon the fauces may occur, and the relapse will aggravate the disease in all respects. Recurrence of diphtheria, after complete recovery from a former attack, is mentioned elsewhere.

III. Affection of Lymphatic Structures in Neck.—Swelling of the lymphatic glands at the angle of the lower jaw is usually the first sign of poisonous infection spreading beyond the fauces. This is the case even if the glandular swelling precede the appearance of false membranes on the fauces, in which case the mucous membrane of the throat is infected by microbes, although they have not gone on to the formation of false membrane; or, as sometimes happens, false membrane may have been formed in some situation where it is not visible; for example, on the back of the soft palate. But it is seldom that lymphadenitis precedes visible pellicles on the fauces.

The degree of the glandular swelling is proportionate to the virulence of the angina faucium, but not always proportionate to the malignity of the disease; or, in other words, the most malignant form of diphtheria, which kills the patient by intense toxæmia, is not by any means always accompanied by much affection of the fauces or swelling of the neck. In bad cases swelling of the connective tissue around the glands occur; it may be to so great an extent as to deform the whole neck from ears to collar-bones, to render the enlarged glands hardly perceptible, and even to involve the cheeks and upper part of the chest. This external swelling is sometimes tender to touch, sometimes not; it does not pit upon pressure; the skin is either pale or reddened. Erysipelatous redness of the skin over the swelling will sometimes give rise to an appearance closely resembling that of an abscess. Great swelling of the neck is sometimes associated with very great swelling of the fauces; in this case the false membrane is often thin and delicate, the disease showing

itself chiefly as swelling. Much coryza, with irritant discharge, is common. The malignant swelling occurs rapidly; it may be great on the third day of the disease; and death, mainly from dysphagia and dyspnœa, may ensue on the fourth day. The dyspnœa is sometimes particularly great, the frequency of respirations being nearly one hundred a minute; post-mortem the lungs are excessively inflated with air, and yet without any false membrane in the air-passages.

The external swelling is useful as a prognostic sign; if the pellicular formation be not extensive, much affection of the glands and cellular membrane of the neck indicates a virulent form of disease. It is said that the virus of the bacillus diphtheriæ does not cause more than a very moderate degree of lymphatic glandular swelling, and little or no infiltration of the cellular tissue, and that the severer form of affection of the neck (cynanche cellularis) is due to the virus of micrococci.

Suppuration of the lymphatic glands, or around them, is uncommon. The more virulent forms of the disease are fatal too soon for suppuration to occur. In cases which end in recovery, if there be any suppuration, it is slow and scanty.

IV. Some rarer local lesions, that is, of the mouth and salivary glands, attending diphtheritic angina faucium.

(*a*) The parotid and submaxillary salivary glands sometimes suffer in diphtheria, probably in consequence of inflammation spreading from the mouth. The submaxillary glands especially may be felt to be distinctly enlarged, and the parotid swelling, in rare cases, is sufficient to resemble the swelling of mumps.

(*b*) The mouth does not suffer severely; the tongue is furred more or less; the gums are somewhat swollen, and either pale or red, with a very thin film of fur upon them; sometimes they bleed a little, but nothing like the "scorbutic gangrene" described by Bretonneau (3) is ever seen in England at the present day. Small herpetic aphthæ are sometimes present, and now and then a patch of false membrane upon the lip or cheek.

The signs of diphtheria which has spread from the throat to the nose or larynx will be described under the heads of nasal diphtheria and diphtheritic croup. The laryngeal affection, when it supervenes upon disease beginning in the fauces, usually begins within three or four days from the onset of the angina faucium, and seldom after a week or eight days. Post-mortem, laryngeal false membranes are seldom found to be continuous with those in the pharynx. If the diphtheritic angina be of a malignant type, the supervention of croup does not obviously change the aspect of the case; the patient dies just the same, from debility and not from suffocation.

V. Temperature of the Body.—Diphtheria, at its onset at least, is probably always a febrile disease. The fever follows no constant type or course; as a sort of rough rule, it may be said that the fever of the onset falls on the second or third day, and that a moderate rise of temperature continues a few days longer. The temperature seldom rises

above 103° or 104° F., even at the beginning of the disease; when the sore throat is at its height, temperatures about 101° are more common. Diphtheria is not a very febrile disease, and the slighter forms are more febrile than the severer. Indeed, in bad cases the temperature is not only not raised, but is even depressed, temperatures between 97° and 98° being common; in the most malignant cases a temperature of 96° in the rectum has been observed. The cause of such algidity is uncertain.

VI. Albuminuria.—The urine, if it be often and carefully examined, will be found in very many cases to contain albumin. This albuminuria depends upon nephritis, which is in turn due to a soluble poison circulating in the blood.

Albumin first appears in the urine at any period of the disease before the tenth day, seldom later. Albuminuria will sometimes come on copiously, and for the first time, after the throat has seemed to have been free from disease for several days. If the patient survive, albuminuria seldom lasts long, even if it have been great. In a few cases it may persist for some weeks after all other symptoms of disease have passed away. Now and then albumin seems likely to be permanently present in the urine, though whether the albuminuria is really permanent, or whether in such cases the patient's kidneys were certainly sound before the attack of diphtheria, speaking from my own experience, I cannot be sure.

The amount of albumin affords no trustworthy prognostic sign. The urine may be highly albuminous one day, and two or three days afterwards contain the merest trace of albumin. Other things being equal, a case with albuminuria is more serious than a case without it; more patients die who have albuminuria than those who have it not, yet patients will die who have never had it, and patients will easily recover whose urine for a short time has been highly albuminous.

If the nephritis be severe, the urine is scanty and very albuminous; casts and corpuscles are found by the microscope; casts hyaline, granular, and corpuscular: cells having the characters for the most part of leucocytes, but some probably being renal epithelium; a few red blood discs are seen. The urine is seldom or never smoky or bloody. Complete suppression of urine is observed at the end of life in cases which prove fatal by vomiting and heart failure.

Dropsy occurs very seldom, if ever. Symptoms which can without doubt be attributed to uræmia are not met with.

VII. Hæmorrhages and Changes in the Blood.—In some cases of malignant diphtheria the affection of the blood is so profound that during life the lips and even the whole surface of the body are of a slaty-grey colour, quite apart from any dyspnœa or mere respiratory lividity. The blood itself is of a dirty brown colour, which has been compared to prune juice or Spanish liquorice. The nature of the very obvious change which the blood undergoes is but ill understood. (For Leucocytosis, *vide* p. 999.)

Hæmorrhagic tendency shows itself now and then; whether dependent upon changes in the blood or blood-vessels, or both, remains unknown.

Small specks or larger blotches of extravasated blood appear in the skin, mucous membranes, serous membranes, and retinæ. Free bleeding from the mucous membranes occurs, especially from the nose, but also from the throat, stomach, and bowels; the bleeding may prove fatal, either very speedily or more slowly. Hæmaturia is a very uncommon event even in hæmorrhagic diphtheria. The spleen is sometimes enlarged as in purpura, and sometimes not. Hæmorrhage, even when too scanty to be the cause of death, will do much towards increasing the weakness of the patient; such cases are always to be deemed serious.

The hæmorrhagic tendency bears no proportion to the affection of the throat; indeed, the latter may be so slight that the diphtheritic character of the disease shall be wholly overlooked, and the death of the patient be certified as due to purpura hæmorrhagica.

Cerebral hæmorrhage of the same nature is a cause, but a very uncommon cause of hemiplegia.

VIII. Failure of Heart.—In diphtheria the function of the heart is more apt to fail than in any other virulent disease which we meet with in our country. This primary debility of the heart (vital debility, lipothymia), not due to exhaustion of the powers of the whole body, but to a peculiar operation of morbid poison upon the heart itself, which is selected as it were for this effect, constitutes the primary or protopathic malignity of the older writers (Stoll, for example)—the word malignity being used in a much more restricted sense than that referred to on page 1002. The cause of the heart failure is interstitial myocarditis with granular and hyaline degeneration of the muscular fibres. It is probable that similar changes occur in the cardiac branches of the par vagum, and in the plexuses.

A sign of this affection of the heart is found in the pulse, which becomes small and weak, and often irregular. In some cases it becomes more and more frequent, in others more and more infrequent; a high degree of either condition is dangerous, and especially infrequency. The temperature of the body falls even as low as 95·5° in the rectum; the skin and limbs are cold. The first sound of the heart is weak or quite inaudible, sometimes a systolic murmur at apex or base springs up. Unpleasant fluttering or palpitation of the heart may be complained of, and the weakened pulmonary circulation may be indicated by shortness of breath. The face becomes remarkably pale. The patient is sensible of great muscular weakness, is very sluggish, dislikes to be moved, and even takes food unwillingly.

These symptoms often come on gradually, the patient's heart steadily becoming weaker and weaker; patients of this kind may lie a week or ten days in a state of prostration. But the symptoms sometimes set in suddenly, all at once faintness (lipothymia, collapse) occurs, attended by a marked change (which cannot be described) in the look of the patient's face, and by the aforesaid signs of heart failure. The patient may die suddenly and unexpectedly, but usually he lingers for some hours in a state of extreme prostration, consciousness is retained to the

end, and the power of the voluntary movements is in remarkable contrast with the weakness of the heart-muscle.

Failure of the heart is usually met with during the height of the diphtheritic disease, say at any time between the fourth and fourteenth day. A slight affection of the throat may be followed by serious disorder of the heart. When the heart fails later it is usually, but not always, associated with paralytic symptoms.

Signs of dilatation of the heart and systolic murmur sometimes occur during convalescence, and may be expected to disappear when the health of the patient is fully restored. If endocarditis and pericarditis ever occur as a result of diphtheria they are probably dependent upon streptococci.

IX. Vomiting.—Another serious symptom, and one often associated with cardiac failure, is a tendency to vomit. The cause of it is not always the same. But whatever it be, repeated vomiting is a dangerous symptom; most of such patients die in a state of heart failure and algidity within a few hours or a few days.

In very rare cases vomiting is a sign of diphtheria of the stomach.

In most cases vomiting is associated with affection of the kidneys. Sometimes the urine is highly albuminous and scanty, or even completely suppressed; the diminished secretion is probably in greater part dependent upon the vomiting. Sometimes the quantity of albumin in the urine is small; sometimes the renal affection is manifested more by corpuscles and casts in the urine than by much albumin. The patient retains consciousness. Convulsions in rare cases precede death.

Now and then vomiting occurs late in the disease, in the course of paralysis, four or five weeks from the onset of diphtheria.

X. Paralysis.—The period at which paralysis occurs in the course of diphtheria is uncertain and very variable. Palsy sometimes sets in while the primary disease (the formation of false membrane) is progressing, say as early as the fourth day. On the other hand, as much time as ten weeks may intervene between the onset of the diphtheria and of the palsy. The mean interval, computed from many cases, is three or four weeks. More often than not paralysis may be called a sequel of diphtheria; that is to say, a period of convalescence intervenes between the primary disease and the paralysis.

Diphtheria of the fauces is by far the commonest primitive lesion. About one-tenth of all cases of diphtheritic sore throat are affected by paralysis sooner or later. It mostly begins after the second week of the angina; it may occur much earlier, as mentioned above; seldom later than the seventh week. (Paralysis after nasal diphtheria is referred to farther on.)

The usual course of the palsy is this, that it gradually increases until the patient dies, or until the disease begins to decline as gradually as it arose. In the latter case recovery is complete.

There is no constant proportion between the severity of the primary disease and of the palsy; or at least paralysis often ensues when the

primitive diphtheria has been very slight. Indeed, in some cases the sore throat altogether escapes observation, the paralysis being the first evidence of diphtheria.

The fauces, and especially the soft palate, usually suffer first. The signs of palsy of the soft palate are two: the voice becomes nasal, and drinks are apt to return through the nose; moreover, the patient can hardly blow out a candle, inflate the cheeks, suck, or gargle. The palate will be seen to have lost its arching, and to hang straighter than natural on both sides. The sensibility of the mucous membrane and the reflex movements are more or less diminished. These signs are sometimes more marked on the one side of the palate than on the other; or they may even be present on one side alone. Palsy, insensibility, and abolished reflex by no means always concur: one or more of these symptoms may be absent; for instance, the reflex may be lost though sensibility is retained. Paralysis of the lowest constrictor of the pharynx is indicated by entry of food into the glottis, causing choking and cough.

Paralysis is often confined to the fauces and spreads no farther; in this case it will last ten days or a fortnight, and then begin gradually to disappear. The fauces sometimes escape even though the limbs and trunk are severely affected. Sometimes paralysis diminishes in the fauces as it increases in the limbs.

Paralysis of the rima glottidis is indicated by weakened voice and inefficient cough, both dependent upon imperfect closure of the glottis. Together with the paralysis go insensibility and deficient reflex of the epiglottis and interior of the larynx. Hence great danger of pneumonia from entry of food into the windpipe; great danger of suffocating bronchitis also, from deficient expectoration. Recovery from laryngeal palsy is possible.

Paralysis of the limbs affects the legs before the arms; indeed the arms often escape. When the patient is able to walk at all the gait is staggering: at last he may become unable to stand, or even to move the legs in bed. Palsy of the limbs usually takes about seven weeks to reach its height. The muscles tend to waste, and sometimes waste greatly—partly in consequence of the nerve disease, but partly in some cases from insufficient feeding. The electrical reactions of the nerve-trunks are normal. The excitability of the muscles to faradisation is diminished or even wholly lost; voluntary power is sometimes much lessened while faradic excitability remains normal; in some instances faradic excitability will go on diminishing while voluntary power is increasing. The degree of galvanic excitability of the muscles is uncertain; it is often diminished or slow, may possibly be increased for a time, and sometimes, not always, there are qualitative polar changes. Abnormal electrical reactions can sometimes be discovered long after voluntary power over the muscles has been completely restored. Sensibility is mostly retained; when lost it is seldom lost higher up than the knees. Patellar reflex is abolished as a rule, but is sometimes retained even when the palsy is great. On the other hand, patellar reflex is sometimes lost

for a considerable time during or after diphtheria, although the legs never show any weakness. When the reflex returns it has been noted, in a few rare cases, to be excessive for a time, and to be associated with ankle-clonus. The palsied limbs are sometimes painful. Recovery of the proper use of the limbs, and of normal electrical reactions, will certainly occur if the patient survive. But the time necessary for recovery is often considerable, and may amount to six or eight months or more.

The hemiplegia which happens now and then in the course of diphtheria is a different form of disease, being due either to cerebral hæmorrhage or to embolism of the cerebral arteries; in the latter case the source of the embolus is not always discovered.

The muscles of the trunk sometimes suffer in the ordinary form of diphtheritic paralysis, but the case is not rendered more serious thereby unless the diaphragm and intercostals be paralysed. A cause of death is paralysis of the respiratory muscles. The sphincters are very seldom affected.

The eyes sometimes suffer. The commonest affection is dimness of sight, due either to asthenopia consequent upon paralysis of the ciliary muscle (cycloplegia), or to amblyopia consequent upon retinal insensibility and contraction of the field of vision; in the latter case glasses are useless. Any form of ophthalmoplegia externa, indicated by diplopia or squint, is less common. Incomplete blepharoptosis has been observed. The pupil is unaffected, or at most but somewhat dilated and sluggish.

Incomplete palsy of the tongue, lips cheeks, are not uncommon (5). The failure of the heart is in some cases perhaps of a neuro-paralytic nature.

In children and in some epidemics death is not seldom the end of diphtheritic palsy. When death does not ensue complete recovery is certain sooner or later. The duration of paralysis in cases of recovery depends much upon the extent of the affection. When confined to the soft palate recovery may be expected in two or three weeks; when the limbs are affected the duration will probably be three or four months. A duration of eight months, or even more, has been noticed in rare cases. Excluding cases of heart failure, death is due to either laryngeal or respiratory palsy. Laryngeal palsy causes death through inability to cough and to expectorate properly, the result being accumulation of mucus in the lungs. Death is seldom due to impaction of a morsel of food in the larynx. Pneumonia from the entry of smaller particles of food into the windpipe is a much more common event, especially in cases of tracheotomy, or of anæsthesia of the glottis.

When paralysis follows nasal diphtheria the fauces may be unaffected, while the limbs suffer severely.

Although good observers have found changes in the medulla oblongata and spinalis in cases of diphtheritic palsy, yet the prevailing opinion is that the chief and often the only cause of the paralysis is multiple

neuritis. The cause of the neuritis is the specific poison; the palatal palsy which follows palatal diphtheria looks like a purely local effect of the poison.

XI. Eruptions.—Besides the purpura and erysipelas which have been already referred to, erythema and urticaria of no constant or peculiar characters have been observed in patients who have not been treated by antitoxin injection. Suffusion of the skin, almost scarlatiniform, is common.

XII. Arthritis.—Rheumatoid affection of the joints has been observed in rare cases and in some epidemics.

Diagnosis of Diphtheritic Sore Throat.—Diphtheritic sore throat is not in all cases attended by the formation of false membrane, and is therefore sometimes indistinguishable by the naked eye from simple or catarrhal sore throat. The proof of this assertion is afforded by two facts: First, that the diphtheritic bacillus has been found to exist upon the mucous membrane of throats which were, to the naked eye, simply slightly reddened and swollen. Next, observations made in epidemics of diphtheria have rendered it certain that the disease is sometimes transmitted by cases which have the characters of simple catarrhal or inflamed sore throat. (See Latent Diphtheria, p. 1026.)

But the diagnosis of diphtheritic sore throat relates mainly to the false membrane. Inasmuch as not all sore throats accompanied by false membranes are diphtheritic, we endeavour to distinguish the different kinds of pellicular angina faucium. To obtain as correct an opinion as possible concerning the nature of the disease we must invoke the assistance of bacteriology. For obvious reasons, practising physicians send a sample of the morbid growth or secretion to be reported upon by a pathologist who is skilled in the cultivation and discrimination of microbes. But diphtheria is a rapidly progressive disease which demands instant treatment; and for the immediate needs of practice a naked-eye examination of the throat must be relied upon. The bacteriological report often arrives too late; moreover, it is sometimes indecisive or even erroneous; and they who are most competent to give opinions upon microbiology will be the first to admit the predominant value of simple inspection of the patient's throat. It is in this spirit that the following remarks upon diagnosis are written:—

1. Many vesicants and escharotics, when applied to the fauces, produce appearances which closely resemble diphtheria. Cantharides, lunar caustic, nitric acid, liq. ammoniæ, carbolic acid, white precipitate, hot chestnuts or potatoes, boiling water or steam, may be mentioned as instances of such irritants. The diagnosis in many cases cannot be made from the look of the throat alone. The conditions which led to the pellicular inflammation must be known.

2. The disease (or rather the diseases) which in England is most commonly called follicular tonsillitis demands very careful consideration in regard to its relation with diphtheria. Many cases of this follicular tonsillitis are diphtheria in an early stage, the appearance of ulceration

round the mouths of the tonsillar crypts being due to false membrane, which often is first formed in that situation. The membrane may spread afterwards so as to cover the greater part of the fauces in two or three days. In other cases the membrane does not spread upon the fauces, but laryngeal diphtheria is associated with the tonsillar affection; in others, again, the membrane does not spread in any direction, and the true nature of the disease becomes apparent only when the patient infects another person with manifest diphtheria; or the reverse may be the case, that the disease conveyed from a person suffering from manifest diphtheria will take on the form of follicular tonsillitis in the infected patient. But although in all these cases there can be no doubt concerning the diphtheritic nature of the follicular tonsillitis, yet it seems to be equally certain that in other cases the disease is not diphtheritic, those, namely, which show no contagious tendency. But admitting this distinction, it can seldom be drawn from the first examination of a given patient, and therefore in practice it is wise to consider the disease to be in all cases probably, or at least possibly, diphtheritic.

3. Herpes, of the same nature as herpes labialis, may affect the palate so as to produce the appearance of one or more small false membranes which show no tendency to spread after they have once been formed. The diagnosis (not always certain) is much helped by the concurrence of herpes on the tongue, cheeks, or lips.

4. A fungus (blastomyces albicans) sometimes affects the fauces, and causes them to be covered by a growth which looks like a false membrane, and may be so extensive as to cover the soft palate and tonsils. Compared with the false membrane of diphtheria, the growth is of a purer and more opaque white colour; it is much softer also, and when once it has been removed by detergents it seldom reappears. Microscopic examination is easy and decisive.

5. A fungous growth (leptothrix buccalis) sometimes occurs within the crypts of the tonsils, and, coming to the surface, stimulates follicular tonsillitis. Or the growth may spread over the tonsil so as to form a white patch. The chief distinction from blastomyces and pellicular diseases is to be found in the fact that the leptothrix affection is essentially chronic.

6. At any time during the first week of scarlet fever false membrane may appear upon the fauces. This membrane is due to micrococci, and does not afford the Klebs bacillus. Yet by the unaided eye the exudation, which is sometimes abundant, is not to be distinguished from that of diphtheria. The diagnosis depends mainly upon the eruption. The scarlatinal false membrane is very much more prone to be followed by ulceration than is the diphtheritic, and the lymphatic glands are much more likely to suppurate. It is quite true that scarlet fever does not often affect the larynx, yet in rare cases of that disease false membrane may be found even there. Subsequent paralysis does not occur. True diphtheria may complicate scarlet fever during the second or third week, and may occur in scarlatinal nephritis at any stage.

7. The mucous tubercles of syphilis, when they involve the fauces and before ulceration sets in, may resemble diphtheria closely.

8. In rare cases of typhoid fever and early in the disease, false membrane forms upon the fauces; it does not last for more than a few days, but it cannot be distinguished from diphtheria until the course of the disease is manifest.

It seems unnecessary to do more than refer to the faucial affections of small-pox, chicken-pox, and pemphix. The ulceration of tubercular angina faucium is sometimes at first mistaken for diphtheria. And the same is true of that very uncommon disease, primary gangrene of the fauces.

Recurrent Pellicular Angina.—Some forms of pellicular angina are very prone to recur, and the recurrences may be frequent; for example, once every two or three months for a year or two, or even as many as four attacks in twelve weeks. This recurrent pellicular angina is often a very febrile disorder, is not attended by albuminuria, nor followed by paralysis. The nature of the disease, which is not the same in all cases, can be determined by a bacteriological examination only. When the recurrences are frequent, it is probable that a contagium vivum lurks about the throat in an active state. In many cases the disease is but slightly, if at all, contagious.

An attack of true diphtheritic sore throat does not protect against recurrence of the disease. Yet as a rule (which, however, does not always hold good) recurrent diphtheria is not so severe and dangerous as the first attack.

Prognosis.—The prognostics which may be derived from individual symptoms will be found scattered through the preceding pages and need not be repeated here.

The cause of death differs in different cases. (i.) Suffocation by extension of disease to the larynx is common. (ii.) Poisoning of the blood (malignant diphtheria) is a less common cause of death. This malignity is indicated by nasal discharge, glandular swelling, erysipelatous redness of the skin over the swelling, tendency to hæmorrhage, failure of the circulation (as shown by a bad pulse, pallor, and coldness of the surface), and delirium. Death is often sudden. (iii.) Heart failure. (iv.) Palsy of respiratory muscles.

Recovery of the former state of health is sometimes a very slow proceeding, even excepting the cases of paralysis.

Bacteriological examination of the secretions of the fauces will sometimes detect specific bacilli weeks or even months after the patient has seemed to become quite well. No law compels such a person to forego his freedom for the somewhat imaginary good of the public. In these and other similar circumstances the physician must be content with less than strict scientific truth. At any rate, a patient who feels in perfect health and is eager to resume his business will not be deterred by warnings about latent bacilli in his throat. He may even suspect the good faith of his adviser.

Treatment.[1]—As soon as a patient is believed to be suffering from diphtheria, he must be injected with a full dose of antitoxin. We need not wait until our opinion is confirmed by the microscope, for an unnecessary use of antitoxin will do no harm.

Should there be any inevitable delay in beginning specific treatment, we must aim at disinfection of the primary disease, which is usually that of the throat. Both laboratory experiments and clinical experience point to carbolic acid as the best germicide. It may be used in a solution as strong as 20 per cent in the case of children, and 30 per cent in the case of adults. Glycerin or castor oil is a good solvent for the acid. Remove as much of the false membrane as possible by means of some close soft material ("molleton" is suitable) tied on the end of a probe or an osier twig, or held by forceps, and afterwards apply the carbolic solution freely to the denuded surface. Should the false membrane continue to form and to show signs of spreading, the treatment may be repeated once or oftener, according to the discretion of the physician. These applications to the throat tend to exhaust the strength of the patient, and the doctrine of local disinfection may be carried out in practice to a dangerous length. The frequent use (for two or three minutes every hour) of a spray of a saturated solution of boric acid is always serviceable, whether the throat be also swabbed with carbolic acid or not. If deglutition be painful it is well for the patient to benumb his fauces by means of ice before attempting to swallow. When the antitoxin treatment is begun, any local treatment of the throat is unnecessary.

The most important part of general treatment consists in feeding the patient, and milk is the most suitable article of food. It should be given every two hours by day, and every three hours by night. Brandy is useful and even necessary in many cases, especially if an insufficient quantity of milk be taken, or if the patient be exhausted, or if the heart show signs of failing. Should the patient refuse or be unable to take the necessary quantity of food, he must be fed by means of a soft catheter passed through the nostril into the œsophagus.

It is not possible to lay down any universal rule concerning the employment of drugs. None are specific, and the indications for their use must be left to the judgment of the practitioner who is directing the treatment of a case. Chlorate of potash is cleansing to the mouth, but to give the salt in large doses is useless or even dangerous. The old-fashioned chlorine mixture[2] is the best way of giving the chlorate.

[1] For the Serum Treatment refer to p. 1027.

[2] Put thirty grains of powdered chlorate of potash into a pint bottle, and add a drachm of strong hydrochloric acid. Keep the bottle corked until the effervescence has ceased; then add an ounce of cold water and shake the bottle well, not allowing the gas to escape; then add another ounce of water, and again agitate well, and so on until the bottle is full. The resulting solution does not taste nearly so badly as it smells; a little sugar may be added. A tablespoonful or two, according to the age of the patient, may be given frequently. An adult may take the whole pint in the day. Chlorine vapour was recommended by J. Johnstone as early as 1779.

Signs of heart failure should be carefully watched for. If they appear the patient must be kept as still as possible in the recumbent position, and he must not be allowed to sit up, still less to get out of bed, for any purpose. Alcohol and strychnia are the best medicines.

If there be any signs of laryngeal paralysis the patient must be fed by means of a tube through the nose, and by nutritious enemas. The use of the tube is favoured in most cases by insensibility of the fauces and pharynx. If vomiting follow the first use of the tube the practice should not therefore be given up, for the vomiting is seldom repeated. The patient must be watched, and if he vomit he must be turned over on his side, with his head low, so that the vomit may not enter the larynx.

Rest in bed, prolonged more or less according to the severity of the primary disease, is believed to be an important means of preventing subsequent paralysis (5).

Treatment of palsy of the limbs is guided by the knowledge that, if the breathing muscles escape and the heart do not fail, the patient will recover. The chief means of promoting recovery consist in rest and in maintaining or improving the nutrition of the whole body. Massage and electricity may be used, but must be used gently. In respiratory palsy faradisation of the phrenic nerve has been known to do good.

Chloride of adrenalin has been strongly recommended in cases of cardiac paralysis. The dose is from five to ten minims of a solution containing one part of the drug in a thousand parts of water, every four hours, or even more frequently. Dr. J. D. Rolleston (5) advises that the remedy should be used in all severe cases of diphtheria, from the beginning, with the view of preventing subsequent heart palsy. The vomiting, the purpuric state, and the nephritis must be managed upon general principles

B. Diphtheritic Croup (Laryngitis)

That is to say, diphtheria which causes primary or predominant laryngeal symptoms is discovered by means of the laryngoscope, or of the expectoration, or of certain indirect signs of the disease.

I. **Laryngoscope.**—The use of the laryngoscope, which is not always easy even in the case of adults, is difficult or quite impossible in the case of children, especially young children. Hence it seldom avails much in the diagnosis of croup;[1] however, in a case of doubtful nature it is always well to try what the laryngoscope can show. A small, warmed mirror can be passed back into the fauces without any attempt to depress the tongue or to draw it out of the mouth, and in this way the epiglottis, at least, can be seen, if there be not much gurgling of frothy mucus in the throat. Should false membrane appear, this is

[1] For exact definition of the word Croup, see *Medico-Chir. Trans. for* 1879, vol. lxxii. p. 27.

enough, but it need not be said that the non-appearance of membrane proves nothing.

II. **Expectoration.**—Children seldom expectorate false membrane before tracheotomy has been performed; ejection of false membrane through the tracheotomy wound is a very common event. Yet even after tracheotomy for diphtheritic croup it may happen that no false membrane will at any time be seen. Adults, on the other hand, suffering from diphtheria strictly confined to the windpipe, will sometimes expectorate false membrane in large quantities, and this even when the dyspnœa is slight and the chief laryngeal symptom is dysphonia.

III. **Signs of Laryngeal Disease.**—In most cases the diagnosis depends upon certain signs which indicate derangement of the laryngeal functions. These functions are two—vocal and respiratory: vocal, that is, the proper and peculiar function of the larynx, the larynx being the organ of voice; respiratory, that is, transmission of the breath, the larynx being part of the windpipe. The signs of disease correspond with these functions. Disorder of the vocal function is indicated by dysphonia; disorder of the respiratory function by laryngeal dyspnœa and laryngeal stridor. To these must be added a third sign, wholly adventitious, allied to voice on the one hand and to breathing on the other, namely, a peculiar stridulous or laryngeal cough.

1. *Dysphonia.*—As the voice is the peculiar function of the larynx, so dysphonia is the pathognomonic sign of laryngeal disease. Dysphonia relates to the quality or to the loudness of voice. (*a*) When the quality of the voice is changed it is called paraphonia, of which hoarseness is the commonest form, being a lesion of the simple glottic sound and not of the articulated voice. (*b*) When the loudness of the voice is diminished it is called aphonia, a term which implies not only absolute privation of voice, but also any degree in diminution thereof. When aphonia is complete the patient can speak only in a whisper—whispering being articulation pure and simple without any glottic sound.

2. There is nothing pathognomonic about the disordered respiratory functions met with in laryngeal disease. Laryngeal stridor and dyspnœa have to be distinguished from other forms of stridor and dyspnœa; and this can be done by determining the presence or absence of certain by-symptoms. (*a*) By stridor is meant a sound which is produced in the windpipe (larynx, trachea, bronchi) by breathing, and which can be heard without auscultation. Stertor, on the other hand, is a sound which breathing produces in the parts above the windpipe. Narrowing of the windpipe is the cause of stridor, and its loudness depends upon the swiftness of the air-currents; hence when the narrowing of the air-passages becomes great, and the air-currents become correspondingly weak, stridor diminishes or even disappears. The peculiar quality of stridulous breathing is a fact which must be taught by experience, and which cannot be described by words. (*b*) The characters and associated symptoms of laryngeal dyspnœa are these:—(*a*) The dyspnœa is chiefly inspiratory or expiratory; usually the inspiratory

movement is much prolonged, but it may happen that the expiration will be at least twice as long as inspiration. (β) The dyspnœa affects the movements of both sides of the chest, inspiratory dyspnœa being marked by powerful contraction of all the inspiratory muscles, and by recession of the yielding parts of the chest, expiratory dyspnœa being marked by powerful and prolonged contraction of all the expiratory muscles. (γ) The breath-sounds heard by auscultation are weakened. (δ) The nostrils dilate during inspiration or expiration, or are permanently dilated. (ϵ) The up and down movements of the larynx (depressed during inspiration) which attend respiration are much increased in laryngeal dyspnœa; similar movements of the lower jaw are sometimes to be seen. (ζ) The radial pulse is withdrawn from the finger during inspiration in severe laryngeal dyspnœa.

3. The stridulous cough (or croupy cough), a most important sign of laryngeal disease, does not admit of being described in words.

IV. Course of Disease.—In a case of diphtheritic croup dysphonia and stridor mostly precede dyspnœa, inasmuch as dyspnœa requires a greater amount of disease than suffices for the production of dysphonia and stridor. The voice is more or less weakened (aphonia) and husky (paraphonia), yet in strict truthfulness it must be said that sometimes the voice is very little affected, or even not at all. The breathing, instead of being silent, becomes dry and husky, characters more marked in inspiration than in expiration. The cough is usually dry and husky; sometimes it is loose; and sometimes there is a loud barking cough (*tussis ferina*); the noiser the cough, the less the obstruction.

Dyspnœa follows, often the day afterwards; but, as a rule, it does not attain a high degree for another day, or even for two or more days after its onset. There are no remissions, worthy so to be called, in the dyspnœa; when once it sets in it abides, except that it sometimes abates shortly before death. Moderate dyspnœa may at any time become suddenly very great so as to demand instant tracheotomy.[1] In adults the dyspnœa comes on later, progresses less rapidly, and is less severe than is the case with children—the reason of the difference being due chiefly to the relatively small size of the glottis in children, but partly to the more powerful inspiration of the adult, and to his smaller liability to collapse of lung.

V. Comitant Symptoms. — 1. The *lividity* of the patient is not exactly proportionate to the dyspnœa. Sometimes there is but little lividity, or even none at all, though the dyspnœa be permanent and at intervals great. Lividity is often due in part to associated pulmonary disease, bronchitis (catarrhal or diphtheritic), congestion of lungs, or collapse.

2. The *fever* is not high. Indeed, the temperature is often normal, or even subnormal, especially when the lividity is great. When the

[1] Should the reader require a picturesque description (in the style of Aretæus) of the dyspnœa of croup, he may refer to Trousseau, who has performed this work once for all (Trousseau, *Clin. Med.* New Sydenham Soc. vol. ii. p. 477).

lividity is not great the temperature may rise to 102° F., or if the fauces be affected, even higher. Scarcely need it be said that tracheotomy interferes with the course of the temperature.

3. The *fauces* often look healthy, but even upon apparently healthy fauces specific bacilli may breed. In some cases small or extensive false membranes will be seen.

4. Puffiness on one or both sides of the *neck* may exist, or even an enlarged gland or two, the fauces being natural.

5. *Albuminuria* is common, yet sometimes there is none even in fatal cases. There is often an excess of flocculent deposit containing leucocytes.

6. Symptoms of the virulent kind, due to poisoning of the blood, do not occur. Paralysis (except, perhaps, glottic paralysis) does not follow diphtheritic laryngitis, yet the patellar tendon-reflex will sometimes be lost for a long time after an attack of membranous croup in persons who were known to have such a reflex before they suffered from diphtheria.

Prognosis.—1. Before the introduction of the antitoxin treatment, spontaneous recovery occurred in a very small proportion of the cases of laryngitis which had been proved to be diphtheritic by the expectoration of false membrane, or by the comitant affection of the fauces. Tracheotomy saved a few lives, and recovery did sometimes occur without tracheotomy. The younger the patient the smaller were the chances of life, for reasons which have been already referred to when speaking of dyspnœa; but even children of less than a year old escaped with life after having expectorated false membrane.

But now the antitoxin treatment renders the prospect of recovery much more hopeful; and the more hopeful the earlier the remedy is employed. A feeble and husky voice and croupy cough will remain for a week or more after the dyspnœa has ceased, both in cases which have undergone tracheotomy and those which have not. The laryngoscope, when it can be used, does not always afford an explanation of these symptoms.

Recovery after tracheotomy is sometimes imperfect, that is to say, the tube cannot be removed; the reasons of this will be given hereafter (p. 1022).

Diphtheritic croup very seldom recurs after an interval of perfect health. The croup which recurs is of the catarrhal and spasmodic kind.

2. Death is due to one of two causes, either to laryngeal or to pulmonary dyspnœa.

(*α*) Laryngeal dyspnœa is a cause of death which is now usually prevented by operation. The duration of cases which are fatal from laryngeal dyspnœa without operation is two, three, or four days from the onset of the croupy symptoms. Unfavourable conditions which aggravate the fatal tendency of croup are infancy and rickets, for reasons which are sufficiently obvious.

(*β*) Pulmonary dyspnœa is due to many causes:—(i.) Extension of

the inflammation downwards into the lungs, the smaller air-tubes becoming choked by false membrane, or more commonly by creamy muco-pus; upon this condition lobular pneumonia (catarrhal or bronchopneumonia) is very apt to supervene. (ii.) Congestion of the lungs, which occurs when the lungs cannot inspire more than from one-fourth to one-half of their normal supply of air. (iii.) Collapse of lungs more or less extensive. (iv.) Acute emphysema (or insufflation) of the front part of the lungs beneath the sternum and the neighbouring cartilages. (v.) Inability to cough and consequent retention of secretions. (vi.) Pneumothorax, which is not uncommon in fatal cases which have undergone tracheotomy.

Pulmonary dyspnœa mostly sets in from four to seven days from the onset of the croup. Hence it is especially seen in cases of operation, because other cases of laryngeal diphtheria by the end of the first week are either dead or recovering. The dyspnœa sometimes becomes very great all at once.

The signs of pulmonary affection are these:—(i.) Increase of fever, especially in bronchitis and pneumonia. (ii.) Physical signs of bronchitis, extensive collapse, insufflation of lungs, or pneumothorax. (iii.) Expectoration from canula becomes more or less abundant or sticky, or even purulent if the patient live long enough. (iv.) The dyspnœa follows one of two courses: (a) Either it recurs, and becomes as great as before, so that nothing whatever is gained by having substituted, by the operation, pulmonary for laryngeal dyspnœa. Consciousness being retained, the patient suffers as much distress after operation as he suffered before it. (β) Or vital debility prevails, there being no great dyspnœa, but the respiration becoming very frequent, and the pulse very small and weak. Lividity steadily increases. The animal functions soon suffer; drowsiness ensues, the patient being almost continually asleep unless disturbed by cough; sleepiness passes into coma and death, which is easy and without dyspnœa.

Tracheal Diphtheria.—Now and then a case will be met with in which the disease is almost limited to the trachea.

The tracheitis is not primary, but is preceded by a diphtheritic affection of the fauces or larynx, which may have been slight or severe. (i.) The primary sore throat may be attended by the least possible exudation, and the laryngitis be indicated by nothing more than a little hoarseness, and perhaps a few shreds of false membrane seen by the laryngoscope. In about seven days from the first signs of illness the patient begins to expectorate casts from the trachea. (ii.) Or, after a severe and regular attack of diphtheritic angina and croup (which will in some cases have rendered tracheotomy necessary), the patient seems to be fairly convalescent, when the disease relapses in the tracheal form, expectoration of false membrane occurs, but no recurrence of angina faucium or of laryngitis.

This tracheal diphtheria often deserves the name of chronic, the patient expectorating casts of the trachea from time to time for two months or even longer from the beginning of the disease. Albuminuria,

amblyopia, and paralytic symptoms may concur. The prognosis is doubtful; some patients die in one way or another, and some survive.

Diagnosis.—1. Catarrhal laryngitis (catarrhal croup) and diphtheritic laryngitis cannot be distinguished during life unless false membrane be coughed up, or be seen upon the larynx or fauces, or unless the diphtheritic microbe be found in the secretions of the throat. Catarrhal croup is never fatal, however severe the dyspnœa be for a time, unless the inflammation spreads to the bronchi so that the patient really dies from suffocating bronchitis. A case of croup which becomes steadily worse is probably diphtheritic. But, on the other hand, what seems to be catarrhal croup may be diphtheria in its slightest form.

2. The respiratory stridor in some cases of catarrhal croup is excessive, and reaches a height of noisiness which is uncommon in diphtheritic croup. This stridulous laryngitis is especially apt to occur in measles just before the rash comes out; the dyspnœa and distress of the patient are great; the rash appears, and the croupy symptoms speedily subside. The croup which occurs in measles from four to fourteen days after the appearance of the rash is a more serious disease; it often renders operation necessary, and is usually laryngeal diphtheria.

3. Spasmodic croup (otherwise spasmodic laryngitis, Millar's acute asthma for the most part, but not laryngismus stridulus, which is quite a different disease) is distinguished from other kinds of croup on account of a peculiarity in the course of the dyspnœa. The onset (as in all sorts of croup) is marked by dysphonia and stridor. Dyspnœa soon follows and attains a high degree, especially in the middle of the night. After urgent dyspnœa has lasted from half an hour to two hours it begins to abate, and soon becomes slight, the dysphonia and stridor continuing. Such attacks of dyspnœa are prone to recur for two or three nights in succession, each fit being less severe than the foregoing. Now and then (but very seldom) diphtheritic croup will take on the spasmodic form, wherefore it is prudent not to be too confident in pronouncing at first upon the benignant nature of spasmodic croup. Laryngismus stridulus cannot possibly be mistaken for diphtheritic croup.

4. When a child has inhaled a foreign body which sticks in the larynx, and when the history of the occurrence of the accident is wanting or untrustworthy, it is easy to mistake such a case for croup. It will hardly be possible to gain any help from the laryngoscope. At the instant of the foreign body entering the glottis urgent dyspnœa occurs, so that an attack of laryngismus is simulated, and the patient may die on the spot. But if he survive, the dyspnœa abates, and then the case simulates croup. The diagnosis sometimes cannot be made until after tracheotomy by exploring the larynx by means of a probe passed upwards through the wound.

5. Exacerbations of dyspnœa occurring in children suffering from pectoral diseases, such as hydrothorax and acute pulmonary consumption, sometimes strongly simulate croup; and the more so when the dyspnœa is attended by a husky cough.

6. In the case of adults the diseases most likely to simulate laryngeal diphtheria are sundry forms of laryngitis, œdema glottidis, laryngeal paralysis coming on suddenly, and hysterical laryngismus. But in adults the laryngoscope is available.

Treatment.—As soon as possible after a patient is suspected to be suffering from laryngeal diphtheria, a full dose of antitoxic serum must be injected. If the opinion be correct, any delay increases the risk of death; if the opinion be incorrect, the injection does no harm. To surround the patient with pure, warm, and somewhat moist air would seem to be indicated by common-sense. The only local application which can be recommended is that of ice or of ice-cold water to the front of the neck. Emetics are best avoided; they empty the stomach of food, and any good they may do to the dyspnœa is very temporary; usually they do no good at all.

When the dyspnœa becomes considerable the operation of tracheotomy or of intubation must not be deferred too long. Either operation removes the laryngeal dyspnœa, but lividity often persists, and pulmonary dyspnœa often supervenes and kills the patient, as has been already described. Tracheotomy is sometimes followed by evils of its own; for example (i.) Emphysema of the mediastinum, due, according to Dr. Champneys, to the fascia being stripped off from the trachea in the operation. (ii.) Pneumothorax and mediastinal suppuration are apt to follow emphysema of the mediastinum. (iii.) Thrombosis, starting from veins injured during the operation, and possibly extending so far as the right auricle. (iv.) Embolism of a large branch of the pulmonary artery, possibly followed by gangrene of the corresponding portion of lung. (v.) Ulceration of the trachea, due to irritation set up by the end of the canula. (vi.) Sloughing or phagedænic ulceration due to septic infection of the wound.

Tracheotomy, although it usually raises the temperature of the body, does not always do so. It is a bad sign when the nostrils act strongly, or when the breathing through the canula becomes sawing or hissing.

Young children after tracheotomy should be fed by means of an india-rubber catheter passed through a nostril into the œsophagus, and the same method should be employed in all cases which show any tendency for the drink swallowed to pass into the larynx.

The tube should be removed as soon as possible, nor is it too early to make the attempt within twenty-four hours after the operation. But sometimes the tube cannot be removed for a long time after, or, indeed, cannot be removed at all. The cause of the difficulty is not always the same. An abundant growth of granulations sometimes obstructs the windpipe about the wound; this is said to be especially the case when the cricoid cartilage has been divided. Cicatricial contraction of the windpipe above or below the wound is another possible cause of obstruction. The trachea is sometimes dislocated backwards, so that the channel of the windpipe below the wound is not continuous with that above. But in many cases it is hard to say what the cause of the difficulty is,

and little or no help can be gained from the use of the laryngoscope. Paralysis of the glottic dilators is an explanation possible in some patients; in some the emotion of fear seems to play a large part in aggravating any distress which follows removal of the tube. In many of these doubtful cases time alone will suffice to cure. S. G.

Intubation

By E. H. E. Stack, M.B.

In 1885 when O'Dwyer (1) first brought this operation into prominence, many hoped it would replace tracheotomy in diphtheria. It was, nevertheless, found unsatisfactory. The introduction of antitoxin has altered the position. The formation of membrane is by it so curtailed, that in favourable circumstances cases which require one or the other operation have a better chance of recovery with intubation.

It must, however, be reserved for those cases which are under immediate medical supervision and in which skilled assistance is at hand; this practically limits its use to hospital work.

Dyspnœa is the only *indication* for intubation; its degree is estimated by the amount of recession, lividity, restlessness, exhaustion, and sleeplessness. If there be expiratory as well as inspiratory dyspnœa the operation should be performed relatively earlier; this also holds good if the child is losing ground even though the dyspnœa is not very severe; whereas if the patient's general condition is improving, although the breathing be still laboured, it is well to stay one's hand in the hope that the operation may be avoided. Intubation may be put off to a later date than tracheotomy, and this alone enables a certain number of cases to escape operation.

The *technique* of the operation is described in works on surgery; it is not, as a rule, difficult when one has had practice; but experience has continually shown that a beginner often fails, and that some seem never to acquire the knack.

It is not of much importance whether the operation be done in the lying or sitting position. Much discussion has taken place as to whether the string should be kept in (2). At the Bristol Royal Infirmary this is always done and no harm has resulted. Some advocate shorter tubes (3) (4) as easier for extubation, using no string, but pushing them out by external manipulations; most, however, prefer O'Dwyer's, as the short ones are too easily coughed out.

The size for age given on O'Dwyer's gauge is inclined to be too small.

After-Treatment.—The disease is still present, and therefore feeding, stimulants, especially strychnine, and antitoxin will still be necessary.

It is best to let the child be quite unrestrained. They expectorate better and are, I think, less liable to pneumonia. We seldom even put

card splints on the arms. There must always be a special nurse in attendance to see that the tube does not become blocked, coughed up, or pulled out.

Feeding should be by the mouth, without a tube if the child can be taught to avoid letting any food pass into the larynx, but in many instances feeding by a nasal tube is necessary. There is no objection to solid food, which is sometimes taken better than fluids; milk-jelly is therefore very suitable. Opium is not contra-indicated provided dyspnœa and restlessness are absent; some advocate it strongly, but personally I never use it. A steam tent is a mistake unless there is a hard, dry cough.

Complications.—Blocking of the tube with membrane or mucus necessitates its removal and cleaning; but fortunately this very rarely occurs. Bronchopneumonia, so common after tracheotomy, seldom follows intubation. It is curious that the toxic cases which are most prone to heart failure are not often those in which dyspnœa has necessitated intubation.

The tube is sometimes coughed or pulled out; this may be a grave event, as immediate dyspnœa sets in again in about 5 per cent of the cases, and the child may die before assistance can be secured. As a rule there is plenty of time, but this danger almost prohibits intubation in private practice.

Sometimes a peculiar flappy sound and a paroxysmal cough indicate a loose piece of membrane below the tube; this will often be expectorated if the tube is removed.

Aphonia is sometimes present after extubation for a week or so, but eventually the voice becomes natural.

Extubation.—Experience is the best guide, but, as a rule, the tube should be removed after about forty-eight hours: the older the patient and the milder the case the earlier can this be done. In half the cases it will be necessary to put the tube in again for another day or two, and this may be required even on a third occasion.

In spite of great care in the original introduction there are always a few cases in which it is very difficult to remove the tube permanently. Injury to the larynx with consequent ulceration is by far the commonest cause of this, but the fear of dyspnœa, and spasm, sometimes associated with a reactionary œdema after removal of the pressure of the tube, are also responsible. I therefore prefer to remove the tube at night, for if the child goes to sleep directly this is done, it is less likely that conditions necessitating reintroduction of the tube will arise.

Very great patience is sometimes required before the tube can be dispensed with—it may take months, but it is hard to see how tracheotomy is going to help, as some advocate.

The cicatricial contraction which prevents permanent removal of the tube will become worse after the larynx is put at rest by tracheotomy.

Some stenosis may be left in children who have otherwise recovered; it generally improves considerably in the course of the next

few years, but during this time there is a great liability to bronchial troubles.

The *advantages of intubation* over tracheotomy are the absence of the scar, the slighter shock, the ease of obtaining the parent's consent, the possibility of waiting longer than in the cutting operation, and, above all, the diminished liability to pneumonia, and consequently the lower mortality. After careful investigation I have decided not to attempt to compare results by means of figures. It is impossible to avoid error where so many factors are present. The diminution of the death-rate is more marked in children under two years than in those above that age. Taking everything into consideration, my impression is that under the most favourable conditions of operating, nursing, etc., the mortality is almost halved by doing intubation as a routine instead of tracheotomy.

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E. H. E. S.

C. Nasal Diphtheria

Diphtheritic membranes in the nose are often associated with diphtheria of the fauces, a combination which usually indicates a severe form of the disease, but not always. Very slight pellicular sore throat, so slight that its diphtheritic nature is doubtful, may be attended and followed by puriform discharge from the nose, the patient in all other respects seeming to be in good health; and yet this discharge will be capable of conveying diphtheria to other people. Still the rule is, as aforesaid, that diphtheria affecting both throat and nose is malignant or pestilent diphtheria.

Diphtheria sometimes affects the nose alone, so far as can be made out. The sign of this form, as of all forms, of nasal diphtheria is stuffing of the nose and a puriform discharge, sometimes offensive, sometimes bloody, and often very irritant to the nostrils and upper lip. The hæmorrhage is sometimes sufficient to weaken the patient, or even to be the cause of death. The redness and swelling may spread from the nostrils so as to affect the whole nose and the eyelids. The swelling is sometimes attended by erysipelatous redness of the skin. Yet it may happen that there shall be no discharge, and stuffiness be the only sign of nasal disease. Very seldom do membranes come away so as to be discovered in the discharge; they can sometimes be seen by inspection of the nasal fossæ, more commonly they are limited to the hinder parts of those cavities.

Nasal diphtheria is sometimes quite a chronic disease, lasting for many weeks.

The glands at the angle of the jaw tend to be swollen, tender, and painful. Should one nostril alone be affected the glands will be enlarged upon the same side.

The general symptoms of diphtheria confined to the nose are usually marked enough, but they are often supposed to be due to a common cold in the head, and are not much attended to. Albuminuria is usually present during the time of the nasal discharge, and even for some time afterwards. Paralysis will follow in some cases, and may present this peculiarity, that the fauces are not paralysed even though the limbs suffer severely.

Nasal diphtheria is to be treated upon the same principles as faucial diphtheria.

D. Other Local Forms of Diphtheria

Otitis media is sometimes diphtheritic, and false membranes are found in the tympanum after death. The amount of associated faucial disease may be considerable or may be slight, even so slight that its nature is doubtful. The signs of otitis are the same as those of other forms of the disease. The diagnosis depends upon the discovery of the specific microbe in the discharges of diphtheria elsewhere. Erysipelas of the ear and neighbouring parts sometimes follows upon rupture of the tympanic membrane. Chronic otorrhœa may ensue.

A portion of the skin which is excoriated or blistered is prone to be attacked by diphtheria in a patient already suffering from that disease; the membrane, if thick, looks very much like a layer of lard. The skin around is often erysipelatous.

A granulating wound is very seldom attacked, the wound of tracheotomy often becomes foul and phagedænic, but anything like false membrane is rarely or never seen.

Conjunctival diphtheria (which is said to be sometimes due to the disease spreading up the lacrimal passages), and diphtheria of the vulva, vagina, anus, or prepuce are diseases very uncommon in England.[1]

The œsophagus is seldom affected. This form of disease affords no characteristic symptoms, and is usually not suspected during life unless a membranous cast be rejected.

Diphtheria of the stomach has been referred to in the section on vomiting.

E. Latent Diphtheria

The diphtheritic poison may affect the throat without being revealed by the formation of false membrane. In this case the mucous membrane is either red, swollen, tender and painful, or it looks quite natural. The former condition cannot be distinguished from simple inflamed or

[1] The reader who wishes for information upon these topics may refer to Dr. Northrup's article upon diphtheria in the American edition of Nothnagel's *Encyclopædia of Practical Medicine*.

catarrhal sore throat, unless there be good reason for believing that the patient has been exposed to the operation of the diphtheritic poison, unless the specific bacillus be found in the secretions, unless the patient convey diphtheria to some neighbour, or unless the peculiar paralytic symptoms follow what seemed to be a common sore throat. After a manifest attack of diphtheritic angina faucium the throat may seem to have returned to its normal condition, and yet the microscope may discover the specific bacillus in the secretions, even after a considerable time (seven months, it is said) has elapsed since the cessation of the disease.

Diphtheria of the larynx is often latent; that is to say, a patient has croup, and from first to last it is impossible to say whether the disease be diphtheritic or not.

Latent nasal diphtheria is either primary or secondary: (i.) A patient has a discharge from one or both nostrils, which is deemed at first to be a simple coryza, and which, if the disease last several weeks, is supposed to be due to syphilis, disease of the turbinate bones, or of the maxillary antrum; and surgical proceedings may be recommended. But the debility of the patient is noted to be greater than the local disease can account for, or the urine is found to be albuminous, or paralytic symptoms occur, and thus the true nature of the disease becomes apparent. (ii.) The latent nasal diphtheria which is secondary to a manifest attack of the disease has been already described.

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S. G.

TREATMENT BY ANTITOXIC SERUM

By W. P. HERRINGHAM, M.D., F.R.C.P.

The result of ten years of clinical experience is now available by which the value of the treatment of diphtheria by the injection of antitoxic serum can be estimated. The evidence is to be sought, first, in individual experience; secondly, in the records of hospitals; and, thirdly, in the statistics of the Departments of Public Health. It is to the second of these to which we turn first, since in hospitals numbers are so large that any risks of chance and of individual bias are avoided, while their conditions ensure a more correct diagnosis, a greater uniformity of environment, and a minuter record than is possible elsewhere.

It might be thought that there would be little difficulty in determining whether the antitoxin treatment is successful or no, for it seems a simple matter by comparing records to decide whether the fatality of diphtheria is lower when antitoxin is given than when it is not. But it soon becomes clear that for various reasons and in various ways this simple test may prove fallacious. In the first place, since the use of antitoxin has now become universal in hospitals, it is seldom possible to compare two large series of cases treated at the same place at the same time, the one with antitoxin, the other without. There are, however, a few instances in which such a comparison can be made.

1. At the Kaiser und Kaiserin Friedrichs Kinder-Krankenhaus in Berlin, in the years 1890 to 1894, there were treated *without serum* 1287 cases, of which 529 died, or 41·1 per cent.

The serum treatment began on March 15, 1894, and between that date and March 15, 1895, Baginsky treated *with serum* 525 cases, of which 83 died, or 15·6 per cent. But in August and September no serum could be obtained, and a few cases in October, November, and December had for the same reason to be treated without it. These numbered 126 cases, of which 61 died, or 48·4 per cent.

Thus in the middle of a period during which, under the serum treatment, the fatality of diphtheria had fallen to nearly one-third of the average, the cases treated on the old methods died at same rate as before.

2. At the Blegdam Hospital in Copenhagen, Fibiger, under Sörensen's direction, divided the cases merely according to the day of admission, treating with serum those admitted on alternate days, while those admitted on the intermediate days were treated without it. The experiment lasted from May 13, 1896, to May 13, 1897, and was carried out as arranged, except that toward its close the physicians, who were already driven to the conclusion that the serum had a powerful effect, used it on a few severe cases out of their proper turn. Excluding cases admitted moribund, which died within 24 hours, 483 cases in all were treated—

238 with	serum, of which	7 died, or	2·94 per cent.
245 without	„ „	30 „ „	12·2 „
483			

Of the 238 cases treated with serum—

203 were pharyngeal, of which	4 died, or	2 per cent.
35 „ laryngeal, „	3 „ „	8·57 „

Of the 245 cases treated without serum—

200 were pharyngeal, of which	14 died, or	7 per cent.
45 „ laryngeal, „	16 „ „	36 „

Of the 238 cases treated with serum—

72 had albuminuria.
37 „ paralysis.

Of the 245 cases treated without serum—

75 had albuminuria.
36 „ paralysis.

It would hardly be possible to find two sets of cases more strictly parallel than these. The total death-rates are small compared to those of other hospitals, because they are calculated without the "moribund cases," which always form a large proportion of the total deaths. In both Baginsky's and Fibiger's cases the clinical diagnosis was confirmed by bacteriological investigation.

3. At the Willard Parker Hospital for Children in New York a similar experiment was carried on for six weeks in 1898. During that time every other case only was treated with serum. In reporting it Park gives no numbers, but writes :—"I carefully watched both series of cases, and the difference was very marked in favour of the antitoxin series."

These, then, are the results with contemporaneous series of cases. But since they are few the critic must further resort to a comparison of the fatality attaching to diphtheria, now when antitoxin is used, with that which obtained before 1894 or 1895. This course, however, is open to several fallacies :—

(*a*) *The Type of the Disease may have altered in the interval.*— Such a change undoubtedly occurs ; thus epidemics of zymotic disease vary greatly in their virulence, and it has frequently been noticed that the fatality of an epidemic is greater when the cases are most numerous than either at the beginning or at the close of the outbreak. Nevertheless, it is highly improbable that an alteration of type would take place abruptly, and a fair critic will accept on this point the judgment of those who watched the disease in both periods.

(*b*) *The Class of Cases treated in Hospitals may have altered.*—In 1894 Behring's discovery drew more attention to diphtheria than it had previously received. There is no doubt that in some diseases, when greater attention is paid to diagnosis, a greater total of cases is returned. I am not at all sure that this would be the case with diphtheria if the diagnosis had continued to rest upon purely clinical evidence. But since this has been supplemented by the bacteriological test there is no question that if every patient is said to have diphtheria in whose throat the bacillus diphtheriæ is found, the average severity of the cases will diminish, since many such are, and remain, perfectly well, and would not have been so diagnosed in former times. In comparing statistics, therefore, it is necessary to be certain that the diagnosis rests upon the same grounds in all.

(*c*) *The other Conditions may not be the same.*—It is, for instance, unsafe to compare strictly the hospitals of one town with those of another. There may be in their circumstances a difference sufficient to account for a difference in their death-rate. And even in comparing the past with

the present rate of one hospital or group of hospitals, it is essential to be certain that there has been no great change in buildings, nursing, or medical attendance during the years included.

It is easy to learn all these particulars at home, difficult abroad. It is for this reason, partly, that I shall use the statistical reports of the Metropolitan Asylums Board as my principal evidence. It is partly, also, because I know no statistics in any language so full, so accurate, so continuous, and so scrupulously impartial as those drawn up by the medical superintendents of the fever hospitals of this Board. The Metropolitan Asylums Board, formed by Act of Parliament in 1867, owes its cumbrous name to its possession of a few asylums for imbecile children. Its most important function, however, is that of providing accommodation and treatment for the chief infectious diseases of London.

Statistics of the Metropolitan Asylums Board Hospitals.—Between 1888 and 1894 the hospitals of the Metropolitan Asylums Board treated 11,704 patients with primary diphtheria. Of this number 3541 died, a fatality of 30·25 per cent. The rate varied in different years, though for the last four it had been stationary.

In 1888 it was 59·35 ; diphtheria was admitted during part only of this year.

In 1889 it was 40·74	In 1892 it was 29·35
„ 1890 „ 33·55	„ 1893 „ 30·42
„ 1891 „ 30·63	„ 1894 „ 29·29

A few cases, not included in the above, were treated with antitoxin in 1894, but it came into general use first in 1895. During the nine years 1895-1903, 55,548 cases of primary diphtheria have been treated, the yearly number varying from 3529 admissions in 1895 to 8225 in 1900. Antitoxin has not been given in every case. In 1895 only 61·8 per cent of the whole number admitted were treated with antitoxin, but the number so treated rose gradually to 81·4 per cent in 1898. I do not find that this record has been published since then, but I believe that the proportion has rather increased than diminished. The cases not so treated are on the one hand the very mild, and on the other those which are admitted moribund.

Under this treatment the fatality has fallen—

In 1895 it was 22·5	In 1900 it was 12·01
„ 1896 „ 20·8	„ 1901 „ 11·31
„ 1897 „ 17·5	„ 1902 „ 10·8
„ 1898 „ 15·5	„ 1903 „ 9·29
„ 1899 „ 14·05	

A detailed comparison of the results of 1894 and of 1895, the latter with and the former without serum,—the few cases treated with serum in 1894 were excluded—was drawn up by the medical superintendents and published in the Report for 1895. The total numbers were much the same, 3042 and 3529 respectively, and the medical superin-

tendents expressly state that the average severity of the disease did not alter. From this Report it appears that under antitoxin not only did the general fatality fall greatly, but that the fall was especially marked in the first five years of life, during which the disease is acknowledged to be more fatal than at a later age. I have added the numbers of 1896 also. The total number under five years of age was—

In 1894,	1171 cases,	of which	556 died,	or	47·4 per cent.
„ 1895,	1453 „	„	477 „	„	34·2 „
„ 1896,	1786 „	„	541 „	„	30·2 „

Although the cases were as severe in 1895 as in 1894, it is probable that the severity has lessened of late years, for whereas in 1896 the Board received only 32 per cent of all the cases of diphtheria notified in London, the proportion has gradually risen to 62 per cent in 1902.[1] It is probable, therefore, that milder cases are admitted now than in the earlier years. But in order to correct as far as possible the source of error, the medical superintendents have each year published separately the statistics of laryngeal cases and of tracheotomies. The laryngeal cases form a dangerous class, and are of a fairly constant degree of severity. In 1894 there were 466 cases, of which 289 died, or 62 per cent. In the nine succeeding years there have been 5657 such cases, the yearly number lying between 491 in 1897 and 799 in 1900. The fatality has been as follows :—

In 1895 it was 42·3 per cent.		In 1900 it was 24·57 per cent.	
„ 1896 „ 29·6 „		„ 1901 „ 22·0 „	
„ 1897 „ 30·9 „		„ 1902 „ 20·9 „	
„ 1898 „ 34·4 „		„ 1903 „ 18·21 „	
„ 1899 „ 29·3 „			

The rate has thus fallen, though not continuously, to less than a third of the rate of 1894.

A still more constant standard is that of tracheotomy. Cases which need this operation are always the most dangerous of all. In 1894 there were 261 cases, of which 184 died, or 70·4 per cent. In the nine succeeding years there have been 2632 such cases, the numbers lying between 180 in 1903 and 390 in 1900. The fatality has been as follows :—

In 1895 it was 49·4	In 1900 it was 34·3
„ 1896 „ 41·0	„ 1901 „ 30·9
„ 1897 „ 40·0	„ 1902 „ 32·5
„ 1898 „ 38·0	„ 1903 „ 32·22
„ 1899 „ 39·1	

[1] I take for this statement the statistics of the Medical Officer of Health of London (Report of Public Health Committee of the London County Council for 1902. Diagram opposite p. 51). The Metropolitan Asylums Board Report for 1903 gives 38·63 and 72·87 respectively (see Table A3, p. 162). The Board is probably considering a rather different total population.

A different but highly interesting piece of evidence is obtained by comparing the cases which were treated early with those which were only seen late in the disease. At the Brook Hospital this comparison has been continuously made. In the six years 1898-1903, during which this hospital has been open for diphtheria—

					Per cent.
181	cases have been admitted on the	1st day of disease,	0	deaths.	
1186	" " "	2nd " "	51	"	or 4·3
1233	" " "	3rd " "	146	"	or 11·03
963	" " "	4th " "	167	"	or 15·2
1260	" " "	5th " "	251	"	or 19·9

These are the results of the antitoxin treatment at the Metropolitan Asylums Board Hospitals. All these figures are for cases of primary diphtheria alone, and in order to compare honestly the treatment with antitoxin with that of previous years, the system of diagnosis by clinical symptoms has been adopted throughout, though bacteriological examinations are made of all cases. It is obvious that the medical superintendents think the clinical more reliable than the bacteriological test, but it does not much affect the numbers. In 1896 the proportion of cases which did not show the bacillus diphtheriæ was but 4·5 per cent of the whole. In the whole number of cases every death is recorded whether due to diphtheria or no. If a patient admitted for diphtheria catches scarlatina while in the wards, and dies of that, the death is entered among the fatal cases of diphtheria. During the whole series of years reviewed there has been little if any change in other conditions. One or two fresh hospitals have been opened, but the treatment has been unaltered, save for the use of antitoxin, and the medical superintendents remain the same.

Statistics so large, so uniform, and so careful as these are sufficient to form a judgment on unless they are contradicted by others. Were this so the difference would have to be explained. But the need has not arisen. There is no country in which with equal opportunity for observation the verdict is not the same. At the Moscow Congress every country in Europe was represented in the discussion on the serum treatment. There was not a dissentient voice. All agreed upon its curative power.

Rauchfuss then brought forward vast statistics from Russia; Sevester from the Hôpital des Enfants malades at Paris, Martin from Geneva, and Escherich from Gratz, gave similar evidence. Rosenthal, by a circular sent to medical practitioners, obtained a very large collection of favourable opinions based upon 12,375 cases with a fatality of but 5·23 per cent, and received from the public health offices of 157 cities in the United States and Europe replies, giving 183,256 cases previous to the use of antitoxin, with a fatality of 38·4 per cent, and 132,548 cases treated by antitoxin, with a fatality of 14·6 per cent. Kossel gives the detailed statistics from Berlin, showing that whereas in the whole city the

fatality of notified cases averaged 30·2 up to the end of 1893, it averaged 14·7 during 1895, 1896, and 1897, and fell to a little lower in hospitals. Biggs (2) reports 3073 cases among very poor people treated at their own homes by the Department of Health in New York, with a fatality of 13·9 per cent. Siegert writes at length on the statistics of the children's hospitals in Vienna from 1886 to 1900. The lowest fatality up to 1894 was 40·6 per cent. Since that date it has never risen above 22·3. Billings shows a similar difference for New York. M'Collom gives the curve of fatality for the Boston City Hospital. In 1888 it was 46 per cent, in 1890 it was 36, in 1893 it was 48, in 1894 it was 38. In 1895 it fell to 14, and has gradually sunk since then to 9·5 per cent in 1904. The total cases are not given. Dr. Cobbett has compiled interesting statistics for nine large British towns, Paris, and Berlin. From every direction the evidence is similar.

In England I cannot hear of any town whose public hospitals do not endorse these results; but the treatment is not so uniformly successful as it is in London, and it is not to be expected that it should be. Not only are the Board Hospitals magnificently equipped and maintained, but also, as it seems, both the public and the practitioners of London co-operate more promptly with the sanitary authorities than is the case in many towns. This is shown by the early date at which in London the cases are admitted to hospital. In London there were admitted *before the fourth day of the disease*—

In 1894,	40·8	per cent of the total admissions.
„ 1895,	32·3	„ „ „
„ 1896,	35·3	„ „ „

But in Manchester Dr. Knivett Gordon, himself accustomed to the Board Hospitals of London, deplores that in the Monsall Hospital, of which he is now superintendent, only 13·4 per cent of his cases are admitted before the fourth day, that over 50 per cent are admitted after the fifth day, and that hardly ever is antitoxin administered before admission.

Not only is all clinical experience unanimous in declaring, as in the Brook Hospital, that an early use of the serum is of great importance, but also pathological theory, founded on experiment, maintains that it is only the free toxin which can be thus neutralised. Dr. Bosanquet writes, "The toxin which has already entered into combination with the side-chains of the tissue-cells is practically beyond the reach of the remedy." Nothing, therefore, can have a greater effect upon the success of antitoxin treatment than the date at which it is employed. When it is not given until late in the disease we may expect it to be of little value. It is so used in a large number of cases in Manchester, and I hear the same report from many of the great towns of England. This then, and such as this, is the evidence of hospital statistics for the success of the antitoxin treatment.

The second class of evidence to which I had meant to turn is that of Public Health Departments, which include disease treated in the home. I thought that in London, or in any large town, the total number of notified cases of diphtheria, compared with the total number of registered deaths from the same cause, would give me fair evidence of the general fatality of the disease, and that by comparing the present with the past it would be possible to make some estimate of the value of antitoxin. This attempt, however, had to be given up for two reasons. In the first place, the notification is too inexact, the diagnosis both here and in the registered deaths too inaccurate to be of value. In London the cases of mistaken diagnosis of diphtheria vary from 7·4 per cent of the whole in 1899 to 14·7 per cent in 1903. These at least were the proportions among the cases admitted to the Board Hospitals (18), which are now more than three-fifths of the whole. Hence if this is the case in London, where, as I have already noticed, great attention is paid to diphtheria, it is not surprising that in other cities, *quas honoris causâ non nomino*, the numbers should rise even to 25 per cent.

In the second place, I am astonished to find that a large number of medical men do not yet employ antitoxin. I have no means of finding out how large this number is, and therefore can draw no valid conclusions from the unclassified returns of Public Health Reports. The same source of error occurs in Germany (13) and America.

To some, however, these considerations have not appealed. De Maurans, and following him Kassowitz, take official public health statistics without question, assume the general use of antitoxin, and argue—(1) That because the total of deaths from diphtheria may fall from other causes, therefore the remarkable fall in the death-rate from diphtheria should not without severe scrutiny be ascribed to the use of antitoxin. This is true. (2) That because in some towns in certain years since 1895 the death-rate from diphtheria has risen, antitoxin cannot have the effect attributed to it. (3) That because in some places the fatality of the notified cases has varied a little since 1895, antitoxin cannot have any specific influence at all. Kassowitz goes so far as to contrast the death-rate of diphtheria since the introduction of antitoxin with that of variola since the introduction of vaccination.

These two arguments rest upon an erroneous interpretation of statistics. The latter has no weight whatever. No specific drug—quinine, for example—cures always the same proportion of cases. Nor is there much resemblance between vaccine and the antitoxin serum. The former is a strong preventive and is almost universally used; the latter is very little used as a preventive, and has but slight preventive power. Vaccine is not a curative, and is never so used; antitoxin is.

Nor is the second of the three of any real importance. The number of deaths depends, first and foremost, upon the number of cases; in other words, upon the extent of the epidemic. Antitoxin could not as now used stop epidemics, and does not. It is used almost solely on cases which are actually infected, and which have already had ample oppor-

tunity of infecting others. Epidemics still occur, and will occur; and with a rise in the case-rate a rise in the death-rate will follow, provided that the rise in the case-rate is large enough to compensate for the fall in fatality, and to leave a few deaths over. Take the London figures for an example—

Year.	Death-rate from Diphtheria per 1000 living.	Case-rate per 1000 living.	Case-mortality per cent.
1891	0·31	1·5	22·5
1892	0·44	2·0	22·2
1893	0·74	3·2	23·3
1894	0·61	2·6	23·6
1895	0·52	2·6	20·4
1896	0·59	3·1	19·3
1897	0·50	3·0	17·0
1898	0·39	2·7	14·8
1899	0·43	3·1	14·2
1900	0·34	2·7	12·8
1901	0·29	2·7	10·9
1902	0·25	2·3	10·8

The death-rate has not fallen continuously from year to year. It rose in 1896 and in 1899. But this is more than accounted for by the rise in the case-rate, or, in other words, by the greater magnitude of the epidemic; the fatality which was stationary, or even rising a little, from 1891 to 1894 has sunk steadily and rapidly ever since. I cite these to show that the death-rate used as De Maurans has used it is unreliable, and that the statistics when fully examined disprove his contention.

Serum Treatment of Hæmorrhagic Diphtheria.—Hæmorrhagic diphtheria, the most malignant form of the disease, was at one time ascribed to a mixed infection, and the use of anti-streptococcic as well as antitoxin serum was recommended (*vide* p. 996). I have never employed this double treatment; but I learn from Dr. Foord Caiger and Dr. Goodall, who have, that it was not successful, and that they had given it up. Dr. Caiger considers that the streptococci or staphylococci act by reinforcing and strengthening the diphtheria bacilli, and that the proper treatment for such cases is massive injection of antitoxin. Dr. J. D. Rolleston, assistant at the Grove Hospital, writes to me in similar terms.

Dosage.—The doses of antitoxin now given are considerably larger than they used to be. At first a few hundred units were given, now several thousand are employed. Some give 10,000 or 12,000 at once; but the best plan is that recommended by Dr. Caiger at the meeting of the British Medical Association in 1904, to give 6000 to 8000 at once, and repeat the same dose every twelve or twenty-four hours until such time as the membrane shall have become definitely shrunken, and be obviously separating. Thus the mild cases get one or two doses only, the severer receive many. The dose should not be regulated by age, but by the severity of the disease.

Bad Effects of Antitoxin Injections.—The injection of antitoxin is often followed by symptoms more or less unpleasant. The commonest is an *erythematous or urticarial rash*, which breaks out from eight to twelve days after the injection. It may be confined to the neighbourhood of the puncture, but is more often general, and it may recur more than once. The itching is sometimes distressing. In a certain number of cases there is pain in the joints, but no sign of any effusion. Arthritis is much less common. It generally lasts a day or two, and is accompanied with pain and effusion. I have thought salicylate of sodium relieved it, but I find others do not agree with me, and the swelling heals quickly by itself. Another rarer, but much more serious complication, is severe pain with or without arthritis, not only in the joints, but in the muscles also. Dr. Newton Pitt has told me of three such cases—a child, his mother, and his nurse—who were for two or three days in such excruciating pain that they could hardly bear anyone to move in the room, and were quite unable to take food. They said that they had never felt so ill in their lives. None of them, as it happened, had diphtheria at all, for the treatment was carried out on a bacteriological report which was afterwards recognised to be at fault. But we have had a genuine case of diphtheria in a nurse, similarly affected, at St. Bartholomew's. Dr. Caiger mentions another instance in a medical man; and a still severer case in which the symptoms lasted more than a month is recorded by Szontagh. In all these affections there may be pyrexia; in Dr. Pitt's case the child's temperature rose several degrees. These sequels do not depend upon the antitoxin, but upon the serum. The stronger the serum the less of it is given, and the less is the liability to the sequels. We, at St. Bartholomew's, have thought that there was a difference in the serums, and that one serum seemed much more likely to produce sequels than another. Adults, so far as I have seen, feel pain after the injection both of antitoxin and of antistreptococcic serum much more than children.

It was at one time alleged that *albuminuria* and *paralysis* were more frequent with antitoxin than they were before.

My own observations, made before antitoxin was introduced, led me to conclude that about 75 per cent of children passed albumin during the disease, but that permanent nephritis was extremely rare. It is not alleged that albuminuria has become more frequent than this, and I do not, therefore, imagine that the use of antitoxin has altered its incidence.

Paralysis.—Dr. J. D. Rolleston, in an exhaustive article, states that the percentage of cases in which paralysis was observed rose after 1894. The yearly rate in the Metropolitan Fever Hospitals as given by him has been as follows:—

In 1893	cases	of paralysis	were	14·2	per cent	of all.
„ 1894	„	„	„	13·1	„	„
„ 1895	„	„	„	20·4	„	„
„ 1896	„	„	„	20·5	„	„

In 1897	cases of	paralysis	were	20·55	per cent	of all.
„ 1898	„	„	„	19·42	„	„
„ 1899	„	„	„	20·0	„	„
„ 1900	„	„	„	18·5	„	„
„ 1901	„	„	„	15·0	„	„
„ 1902	„	„	„	17·07	„	„

He points out that the increased rate is not likely to be due to antitoxin, since (1) the early administration of antitoxin and (2) the use of large quantities evidently tend to make paralysis, and especially the severe kinds of it, less likely to occur. He thinks that more cases are noted now (1) because more cases survive; (2) because greater attention is paid, so that slight cases which formerly passed unnoticed are now registered. Here, as in other points, the lack of large contemporary series of comparison is greatly needed, though, if physicians do their duty, they will never be obtained. Fibigen's statistics given on p. 1028 show that in all probability antitoxin has not altered the incidence of paralysis to any appreciable extent.

In a few cases *death* has been ascribed to the use of antitoxin. Saward describes two cases of syncope following closely upon the injection. They were sisters. One of them died; the other was saved with difficulty. Escherich quotes the case of Professor Langerhans' child, and adds from his own practice another. The latter was a fine boy of eleven months, who, when seized with laryngitis, was injected as a precautionary measure with antitoxin. He died a few hours later with sudden failure of the heart. No morbid condition was found except a very large thymus, 15 grammes in weight, and the same was the case in the late Professor Langherhans' son. Sudden death in children with a large thymus is a well-known occurrence, and it may be that both cases were the result rather of the condition known as lymphatism than of the injection. Yet the possibility of such a death must be remembered. It is, however, of such extreme rarity that it can hardly be reckoned as a danger.

Gerlach describes a case which is, I believe, unique. A girl, three years old, was treated with antitoxin on the fourth day of diphtheria, and was convalescent, when on the eleventh day an erythema appeared and some vomiting took place, followed next day by repeated convulsions, and on the day after by death. Gerlach found multiple hæmorrhages on the outer surface of the dura mater and on the pleural surface of the lungs. He compares these to the exudations in the skin, and thinks they may have been the cause of the convulsions. It seems much more reasonable to regard them as a consequence.

It is as well, however, to quote these instances, in order that, if they are the result of antitoxin, which is very doubtful, they may be supported by others, and the reality of the danger established.

Prophylactic Use.—Antitoxin has been used not only as a curative, but also in a certain number of instances as a preventive. Of its power

in this respect outside the laboratory it is difficult to judge, for the chance of infection must always be hard to determine, and the opportunity to compare parallel series of cases is rare. It is allowed by all that the preventive power of antitoxin is not established under twenty-four hours after injection, and ceases at the end of four weeks. Biggs (2) gives two interesting examples of its use. At the New York Infant Asylum 107 cases of diphtheria occurred in 108 days. Thereupon, on 17th and 18th January, all the children were injected. In the following 30 days only one case occurred, but from 15th February to 27th February there were six cases. On 27th February, therefore, a second injection was made. Thirty days followed without a fresh case; after which five mild cases were observed. At the Nursery and Child's Hospital there were 46 cases of diphtheria between 18th January and 18th April, fifteen of which occurred in April. On 18th April the children, 110 in number, were immunised. No further case was found among them, but an assistant physician and a nurse, neither of whom had been injected, caught the disease in the next few weeks. Netter reports on the same plan of treatment carried out among out-patients, and his statistics, though they include too few cases to allow of a firm conclusion, are yet valuable, because they give parallel cases not so treated. Between 16th March and 31st December 1902 he tried to inject all the children in every family from which a case of diphtheria was admitted into the Trousseau Hospital.

502 children belonging to 251 families were injected.
7 children caught diphtheria less than 24 hours after injection.
6 ,, ,, ,, more ,, 28 days ,, ,,

13 ,, ,, ,, = 2·59 per cent.
10 cases were mild, 3 moderate, none fatal.

491 children belonging to 201 families refused injection.
87 children caught diphtheria = 17·72 per cent.
19 cases were mild, 18 moderate, 12 doubtful, 20 severe, and 18 fatal.

The children were of the same class and resided in the same area, and the two series were as closely parallel as they could be. Slawyk states that the systematic treatment, by injection, of every exposed child has completely stopped the "house infections" which were formerly common in the children's department of the Charité at Berlin. Kraus, from his experience of the results in Ganghofner's clinic at Gratz, is strongly in favour of preventive injection.

This and similar evidence, though not by any means conclusive, affords a fair presumption of the efficacy of the injections. I should certainly advise that in any hospital or school where a few cases, and in any family where even one case of diphtheria had arisen, every child should

be injected with from 300 to 500 units of antitoxin, and that the injection should be repeated at the end of 21 days.

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TETANUS

By the late Professor Sir GEORGE M. HUMPHRY, M.D., F.R.S., and Professor G. SIMS WOODHEAD, M.D.

Revised by Professor G. SIMS WOODHEAD, M.D.

SYN.—Greek, τέτανος (a straining, from τείνω); Latin, *Rigor Nervorum* (Celsus); Germ., *Starrkrampf.*

TETANUS, now generally recognised as a virulent infective disease, is characterised by continued contraction of the musculature of the patient, the spasms commencing in small groups of muscles and gradually extending to those of the whole body, especially the respiratory muscles. This condition appears to result from an intoxication of the cells of the nerve-centres by the products of a specific bacillus—the tetanus bacillus of Nicolaier. Until comparatively recently, 1884, tetanus was usually supposed to be set up by the irritation of peripheral nerves in wounds (traumatic tetanus) in special positions, the irritation of nerves by physical or mental agencies, by cold (spontaneous tetanus),

or by intoxication by certain substances taken into the alimentary canal. Many surgeons, however, even before this date, were fully convinced that the symptoms were due to the presence and action, in the circulating blood, of a special poisonous substance, although they were unable to bring forward any definite evidence in support of this hypothesis. In 1854 the late Sir James Simpson wrote :—" Tetanus is known to follow wounds very various in their degree of severity. . . . The disease, when developed, essentially consists of an exalted or superexcited state of the reflex spinal system, or of some segment or portion of that system." He continued, " We have in obstetric pathology evidence almost amounting to certainty that the analogous superexcitable state of the cerebro-spinal system of nerves which gives rise to eclampsia or puerperal convulsions is generally produced by the existence of a morbid poison in the blood. And it seems not impossible that the generation of a special blood poison, at the site of the wound or elsewhere, may sometimes in the same way give rise to obstetrical and surgical tetanus." He further pointed out that the symptoms of this disease are comparable to those produced by strychnine and brucine. It was, however, found impossible to determine the nature of this poison by clinical observation, and it was not until several years after the publication of Koch's experiments on septicæmia that this poison was proved to be the result of the activity of a micro-organism which had found a nidus in injured tissues. Most of the earlier experiments were directed to the discovery of micro-organisms in the blood, in the lymphatics around a wound, or along the course of the peripheral and central nerves. Simpson says that attempts had been made even before his time to reproduce the disease experimentally by means of injections of the blood of patients who had succumbed to tetanus. So late as 1869 Arloing and Tripier failed to produce tetanic symptoms in the rabbit or dog, by the injection of pus and blood from tetanic patients and horses. They also failed to set up tetanus by the continued irritation of the nerves of various animals.

The experiments of Carle and Rattone (1884), who were the first to demonstrate the transmissibility of tetanus from man to animals; of Nicolaier (1885), who was able to produce the disease with earth or pus containing bacilli which he described but could not obtain in pure cultures; of Rosenbach (1886), who induced a disease similar in most respects to tetanus by the introduction under the skin of the guinea-pig of fragments of tissue taken from the wound of a tetanic patient, and continued the infection with similar results through a series of guinea-pigs and mice; of Kitasato (1889), who was able to obtain Nicolaier's bacillus in pure culture; and of Knud Faber (1890), who produced the disease by the injection of a minute dose of the filtered products of this bacillus—gradually led to the complete proof that tetanus was an infective disease due to the toxic products of a specific anaerobic bacillus.

Tetanus, as pointed out by the late Sir George Humphry, may occur in any person of either sex, at any age; it may ensue from any wound at any part of the body, and in any condition of the wound; or without

any apparent wound. It less often follows wounds of the trunk than of the extremities, and wounds of the lower extremities give rise to it more frequently than those of other parts; but it does not appear that wounds of the feet or hands are more liable to cause it than those of other parts of the limbs. On the whole, however, it occurs more frequently in parts exposed to contact with earth and dirt. It is most likely to occur in cases of severe or lacerated wounds, or when some foreign body is lodged in a simple incised wound, or in compound fractures or burns. It may ensue upon a mere scratch, the wound produced by the beak of a bird, a splinter of wood, especially if a fragment be left in the wound, an old nail, the slightest wound, such as those caused by subcutaneous injections; dilatation of the neck of the uterus by a sponge-tent; after confinements (the post-parturient cases are said to be especially fatal); after cupping; the insertion of a seton; the extraction of a tooth; the injection of a hydrocele; or the plugging of a nostril for epistaxis. In one case, a woman in Addenbrooke's Hospital, the only discoverable local lesion was a chronic ulcer of the leg. It has also been known to take place after complete cicatrisation of the wound. In horses it is said to be caused by wounds in the gums from eating straw or from the pricking of the hoof or of the corona, and cases in the human subject supposed to be idiopathic may have originated in a similar fashion. Sir George Humphry notes that in an early case of ovariotomy in the country, long before the days of antiseptic surgery, all had gone on well, the wound had nearly healed, and he had taken his leave of the patient, when tetanus supervened and proved fatal. He witnessed another fatal case after ovariotomy, performed, with antiseptic precautions, by the late Dr. Meadows. He was of opinion that the disease had been less frequent since the introduction of the antiseptic method in the treatment of wounds; and that this immunity would be still more observable as new methods are more generally and completely carried out, and a more thorough cleansing and quicker healing of wounds effected.

For obvious reasons the disease is more frequent in men than in women, and it is said to be less fatal in women. It is most frequent between the ages of ten and twenty, and is rare after sixty (68). It is much commoner in warm countries than in temperate regions. The bacillus of tetanus grows much more rapidly and luxuriantly and produces a more active toxin at blood-heat than at the ordinary room-temperature of the temperate zone. "It sometimes occurs as an epidemic. Gross says (I do not know upon what authority) that in 1858 it appeared in rapid succession in several of the London hospitals." In this connexion Nocard's early observations (*Bull. de l'Acad. de Méd.* 1889, p. 209) are interesting. He points out the danger of using instruments soiled with pus derived from the wounds of patients suffering from tetanus, and mentions the infective properties of dirty fragments of wood. Macnamara (69) states that in Bengal tetanus has been observed to occur especially after changes of temperature, and that it is rarely absent from the hospitals of Calcutta. He adds that within a period of five years 83 cases were treated in the surgical wards of the Mayo Hospital; of these

44 were traumatic, and 24 (a small proportion) died: of the remaining 39 idiopathic cases 10 died. It is more frequent and more fatal in military than in civil practice. The records, however, of the "Great Rebellion" (see appendix, p. 1077) are more favourable than those usually given of the results in civil practice.

A number of cases of tetanus following the injection of gelatin into aneurysms have been recorded. Wilson describes 52 and MacFarland 95 cases of tetanus following vaccination, all of them occurring in America. In most cases the lymph appears to have been above suspicion, but in the 1901 epidemic of small-pox in Philadelphia, out of 45 cases of tetanus that followed vaccination thirty had been vaccinated with lymph from one source, and MacFarland was greatly impressed by the fact that this lymph had contained tetanus germs, so that even in cases where the tetanus could not be traced to the lymph it may in a certain proportion of cases have had its origin in infected lymph. It is certainly remarkable, and a tribute to the conditions under which vaccine lymph is prepared, and to the much greater attention paid to cleanliness in the case of vaccinated patients, that such accidents are now diminishing so rapidly.

Pathology.—It has already been indicated that tetanus is a specific infective disease, and that it is due to the action of a bacillus. Carle and Rattone found that the virus could be inoculated from man to animals (of twelve rabbits inoculated, all except one were attacked); and they regarded this virus as a *contagium vivum*, probably a bacterium. Shortly afterwards Nicolaier recorded his success in obtaining from pus a virus which he was able to propagate outside the living organism; he also found that certain animals, such as rabbits, guinea-pigs, and mice, when inoculated with particles of soil obtained either from the streets or from cultivated land, became affected by symptoms which he described as tetanic in character and as identical with those met with in tetanus in man. This soil, introduced into a little pocket under the skin, was almost invariably followed by an abscess. The pus in this abscess was found to contain several species of micro-organisms, one of which (although cultivations were carried on for seven generations could never be obtained absolutely pure) he identified as being specially active in setting up tetanic convulsions. He described this organism as a small, slender bacillus, somewhat longer but thinner than Koch's bacillus of mouse septicæmia; he gave no further specific features of identification. In 1886 Rosenbach corroborated and established Nicolaier's observations, by inoculating two guinea-pigs with pus from a tetanic patient, which produced tetanic muscular contraction like that invariably produced by the inoculation of Nicolaier's earth. Rosenbach also produced evidence that one of two bacilli was probably the cause of the tetanic condition: (*a*) a rapidly-growing, thick bacillus, which developed large spores, and had the power of peptonising serum; (*b*) a slender bacillus, which first appeared in the liquefied serum, and then formed spores. He agreed with Nicolaier that the tetanus bacillus was probably the small and slender organism.

It was not till 1889 that **the tetanus bacillus** was obtained in pure culture by Kitasato, and also by Tizzoni and Cattani, who were able to separate the specific tetanus organism, as at present recognised, from the pus of the abscesses occurring in cases of tetanus, and from the tissues immediately surrounding these abscesses. Knud Faber, from investigations carried on about the same time as those made by Kitasato, states that, although he was not successful in obtaining a pure culture of the tetanus bacillus, his experiments support Kitasato's view that the organism is an obligate anaerobe. He succeeded in obtaining from very virulent tetanus cultures a perfectly germ-free filtrate which, when inoculated into animals, reproduced the whole of the morbid phenomena of experimental tetanus.

The organism described by these authors, and now recognised as the specific cause of tetanus, usually occurs as delicate threads, varying in length from 4 μ or 5 μ to slender partially segmented threads of considerable length; these are slightly thicker than the bacillus of mouse septicæmia (one of the smallest organisms known), and the ends are somewhat rounded. Before spores are formed the organism is provided with delicate lateral cilia (50-70 in number), which are continuous with the protoplasm of the bacillus, and pass through a somewhat rigid perforated sheath. From the second to the sixth day of growth these seem to become fewer, longer, and more twisted. From the sixth to the tenth day, as spores are developed, the flagella become still fewer, and branched or with long twisted flagella, which appear now to have taken the place of the delicate or primary flagella. The shorter rods, which up to this stage may have had slight motility, now lose both their flagella and their motility. At blood-temperature spores make their appearance, usually in about thirty hours after multiplication has commenced; but at the temperature of the room they are not observed until nearly a week has elapsed from the commencement of the growth, although the organism continues to grow readily enough at this lower temperature. Until the spores begin to form, the segmentation into short rods may be incomplete; but as soon as sporulation commences the segments become more perfectly marked out, they become motionless, and a clear point is observed at one end of the rod; this becomes larger and larger until it causes marked distension of the end of the bacillus in which it is developed, and thus is formed what is known as the "pin-head" or "drumstick" bacillus. Clubbed and mycelial forms are described by Kanthack and Connell as occurring in gelatin cultivations of this organism. The tetanus bacillus grows best at a temperature of from 36° C. to that of the blood. Below 14° C. it becomes inactive: at 42° C. to 43° C. it also becomes less active, and undergoes what are looked upon as degenerative changes, involution forms being pretty constantly developed. Exposure to a temperature of from 60° C. to 65° C. rapidly kills off the bacillus, but does not destroy the spores, which are exceedingly resistant, even to moist heat, as they can withstand the action of water at a temperature of 80° C. for an hour. Steam at a temperature of 100° C. does not appear to be fatal to them in a less time than five minutes. It is stated

that it requires fifteen hours of treatment with a 1 in 20 watery solution of carbolic acid, or three hours with a 1 per 1000 corrosive sublimate solution, to kill them. Protected from air and light the spore may retain its vitality for as long a period as twelve months, as at the end of that time it appears to be capable, under certain conditions, of developing into the vegetative bacillus. The tetanus bacillus is anaerobic, and grows best in an atmosphere of hydrogen; it appears, however, to be almost as inactive in the presence of carbonic acid gas as in the presence of more than traces of oxygen.

This bacillus is stained by Gram's method. The spores are best stained by leaving them for some time in a 10 per cent alcoholic solution of basic fuchsin, 10 parts, added to 100 parts of a 5 per cent watery solution of carbolic acid. The specimen may be left in this stain for about twelve hours; or the same result may be obtained in two or three minutes if the solution be heated until steam rises from it. The bacilli give up the stain in 25 per cent solutions of mineral acids, but the spores retain it firmly. A contrast stain is obtained by placing the specimen for a couple of minutes in a watery solution of methylene blue. The flagella are well stained by von Ermengem's method or by Richard Muir's modification of Pitfield's method.

The tetanus bacillus has been found in garden-earth, in dust from the streets, or in that taken from between the boards of the floors of rooms, and in the pus from suppurating wounds. It has also been met with in the excrement of animals, especially in that of the horse. Marchesi found that samples of soil freshly gathered often give rise to mixed infections in which the tetanus virus may not appear to play a part; but if to the same soils he added a 5 per cent solution of carbolic acid (which appears to kill most other organisms), he could usually demonstrate their tetanising power; other infections seldom or never occurring. By using this method he was able to produce symptoms of tetanus, not always at the first attempt but often at the second; and he points out that the absence of an infection after the first inoculation does not necessarily show that a soil contains no tetanising organisms.

Amongst certain savage tribes whose powers of observation are usually fairly highly developed in certain directions, tetanogenic soil is the source of one of their deadliest poisons. H. M. Stanley believed that his Central African forest-dwelling pigmies poison their arrows with this death-dealing material, whilst there are records of tetanus poisoning due to wounds inflicted with specially treated arrows from Santa Cruz, the Solomon Islands, the New Hebrides, and New Caledonia. Le Dantéc, speaking of the deaths of Bishop Patteson, Commander Goodenough, and their companions, states that they were all attacked by tetanus, the result of wounds produced by poisoned arrows. These arrows "are about 3 feet in length; the shaft is made of a reed; then comes a middle portion composed of hard wood, and, lastly, a point usually consisting of a fragment of human bone, which is carefully sharpened to a very fine point and is so fixed that it readily snaps off on the

slightest shock. With a sticky substance obtained from an incision made in the bark of a tree, the point composed of the fragment of bone is smeared. The fluid, on exposure to the air, becomes thicker and of a more viscid consistence. Thread is then wound in a spiral direction round and round the sticky point. A quantity of soil from the edge of a mangrove swamp is taken in a cocoa-nut shell or some similar vessel, and into this the arrow-head is plunged. It is then carefully dried in the sun, after which the thread is removed, when a roughened point covered with a film of dry mud and dust is left. In this mud there are probably both septic vibrios and tetanus bacilli; the former, however, are rapidly killed by exposure to the sun, whilst the spores of the tetanus bacillus of Nicolaier may remain active for months or even years." Marchesi found tetanus bacilli in the soil to a depth of two metres; but, below this depth, soils examined by him had not the power of inducing tetanus when inoculated subcutaneously.

It always occurs, then, in these positions mixed with other organisms, and, from the fact that it grows anaerobically, it had, as we have seen, been known to exist for five years before any one succeeded in obtaining it in pure culture. Kitasato, however, at last overcame the difficulty by taking advantage of the fact that the spores of this organism are specially resistant to the action of heat. Taking as his seed material some of the pus from the wound of a patient suffering from tetanus, he made cultures on the surface of agar-agar. At the end of a couple of days he found that a number of organisms had developed on the nutrient medium kept at the temperature of the body; amongst these were the characteristic tetanus bacilli. He then exposed some of the mixture for one hour to a temperature of 80° C.; from the material so treated he made fresh anaerobic cultures, and in a certain proportion of these he found pure growths of the tetanus bacillus. It should be pointed out, however, that certain anaerobic bacilli which may be mistaken for the tetanus bacillus, except that they do not give rise to the tetanus poison, may form spores which are equally resistant to the action of heat. This admixture frequently accompanies the tetanus organism when it occurs in soil: but, as a rule, we are not confronted by the same difficulty when the cultures are made directly from purulent material derived from cases of tetanus.

The bacillus, as we have seen, grows best at the temperature of the body, and anaerobically. It certainly retains its virulence only so long as the free access of oxygen is interfered with; but it is stated that constant cultivation in an atmosphere of pure hydrogen may bring about a fall in its virulence.

It grows readily on any of the ordinary media to which an addition of 2 to 3 per cent of grape sugar, or 0·3-0·5 per cent of formate of soda, is made, even when oxygen is present at the surface of the mass. In gelatin plates kept at the temperature of the room small, slowly-growing colonies with delicate marginal processes are seen at the end of about four days. Under the microscope each colony appears to have a dense

centre whilst the margin is clearer; radiating from the main mass are numerous exceedingly fine threads. In stab-cultures made in gelatin, and kept at a temperature of 21° or 22° C., a growth appears in the deeper part of the gelatin. This has the form of a fir-tree, situated some little distance from the upper surface of the medium, the grey, delicate, fluffy-looking branches getting longer and longer as the surface is left. At the end of the second week the gelatin begins to liquefy, and this liquefaction continues until the whole becomes a cloudy, sticky liquid. After a time the growth sinks to the bottom, leaving the upper part of the gelatin comparatively clear. A similar growth takes place in grape-sugar agar; in this medium, kept at the temperature of the body, the growth goes on much more rapidly, forming spores in a couple of days, and is of course not accompanied by liquefaction. It is a disputed point whether gas-bubbles are formed under these conditions or not. This appears to be entirely a question of the rate of formation of gas; if it is formed more rapidly than it can be diffused through the agar—as in the case of very energetic growth—bubbles may be seen; but this, in my experience, is of comparatively rare occurrence, and the presence of gas-bubbles affords strong evidence of the impurity of the culture. In grape-sugar peptone bouillon the organisms grow luxuriantly, especially at the temperature of the body, and the fluid rapidly becomes cloudy; but after a lapse of six or seven days the upper layers of the fluid become clear, and a greyish-white mass falls to the bottom of the tube. All these cultures have a peculiarly disagreeable aromatic odour, sometimes compared to the smell of burnt onions, with a faint trace of a putrefactive odour.

The Tetanus Bacillus is a Facultative Parasite.—It grows outside the body, and is especially associated with the stable and with manured fields. Sheep and cattle are often affected. The disease is most common amongst agricultural labourers, gardeners, soldiers on campaign, in those who go about with bare feet, or who, like young children, are liable to get their knees or hands accidentally wounded by contact with the ground. It is somewhat important to remember these points, as it has been found that the tetanus organism only retains its virulence under cultivation so long as it is grown under anaerobic conditions; especially is this the case where there has been no time for the development of spores. Even pus from the wounds of a patient suffering from tetanus may be incapable of setting up tetanus infection, the bacilli in these wounds often being placed under conditions unfavourable to the retention of their specific virulence.

Inoculation.—This infective process may be set up in the smaller animals by the insertion under the skin of minute particles of almost any cultivated garden-earth; by inoculation of pure anaerobic cultures of the tetanus bacillus; by the inoculation of spores or a pure culture plus the tetanus poison, or plus lactic acid or bacillus prodigiosus; or by inoculation into a bruised wound. It is worthy of note, however, that the older the culture and the more poison present in it, the greater the

certainty that the disease will follow inoculation. It should be remembered that the tetanus bacillus forms its poison exceedingly slowly, and that the organisms themselves, if unaccompanied by any material which will, as it were, draw off the attention or paralyse the activity of the tissue-cells, are rapidly destroyed by these cells—so rapidly, indeed, that they have no time to form sufficient poison to set up the nerve-changes associated with the disease. Slowly as the poison is formed, however, it is tremendously active, as will readily be grasped when it is pointed out that the five-millionth part of a cubic centimetre of a filtered two to four weeks old slightly alkaline broth culture of the tetanus bacillus—that is, of a solution of the poison formed by these organisms—is sufficient, when injected subcutaneously into a mouse, to kill that animal in twenty-four hours. The lethal dose for a rabbit is about a thousand times this quantity; for dogs five to ten thousand times; and for fowls and pigeons ten to twenty-five thousand or even more times. Metchnikoff points out that spiders and scorpions are very insusceptible to tetanus toxin. Large spiders will withstand a dose that will kill 1000 mice, whilst scorpions will withstand a dose that will kill 5000 times their weight of mice. In their case it is not a question of temperature, for even when they are kept at a temperature of 36° C. no symptoms appear. The injected toxin soon disappears from the blood, which at no stage becomes antitoxic. In the scorpion, however, the toxin may be found in the liver for more than a month after injection. In the larvæ of Oryctes and in the cricket, both of which thrive at a high temperature, the tetanus toxin remains for some time in the blood as proved by its toxic action on mice. Courmont and Doyon observed that frogs are refractory to tetanus in winter, but susceptible in summer. The green frog kept at a temperature of 10° C. remains well after a dose of tetanus toxin which would produce tetanus after a five days' incubation-period in a similar frog kept at a temperature of from 30° to 39° C. By increasing the dose tetanic symptoms may be produced when the frog is kept at from 13° to 18° C., but in such case the incubation-period may run a course five times as long. It is interesting to note that tetanus toxin may be fixed in the nerve-cells, even in animals kept at a temperature of 8° C., without tetanic symptoms making their appearance. If, however, the frog be injected with toxin and kept in a warm incubator for twenty-four hours, and from that be transferred to a cold chamber, no tetanic symptoms make their appearance—the tetanus is arrested even when the toxin has already produced "certain latent but permanent modifications of the nervous system." Further, frogs keep continuously in the cold gradually eliminate the tetanus toxin; if they are kept in a cold chamber for some time, and are then put into a warm incubator, the disease does not appear, or comes on in a very modified form. In the frog as in reptiles, which are very resistant to tetanus at all temperatures, tetanus toxin may remain in the blood for some time—for months; this is proved by the fact that the blood-plasma taken from these animals contains sufficient toxin to kill mice. In spite of, or perhaps associated with, this

long continuance of toxin in the blood in the above animals—no antitoxin is formed. Metchnikoff refers to the presence in these cases of a negative chemiotactic action of the tetanus poison on the white cells of the blood. In the case of the American alligator, however, an animal on which the tetanus poison has apparently not the slightest toxic effect, the toxin is rapidly eliminated from the blood even at a relatively low temperature, 20° C., and the blood does not become antitoxic. But if an adult alligator be maintained at a higher temperature, 32° to 37° C., a certain amount of antitoxin may be developed in the blood, sometimes with very great rapidity, even at the end of twenty-four hours. He mentions a case of the young alligator into which he injected sufficient tetanus toxin to kill 6000 mice. At the end of a month he found that, although the toxin had disappeared, no antitoxin had as yet made its appearance, but at the end of another month antitoxin was found. In these cases the tissues of the animal apart from the blood must be resistant to the toxin; there is no antitoxic power developed as a protective agent, for even in the case of the young alligator the toxin had disappeared before the antitoxin had been found; in fact here we have an example of what Behring terms histogenetic immunity. In fowls, which are highly refractory to tetanus, the toxin may remain in the blood for a considerable period. For blood, drawn from such fowls or organs containing a larger quantity of blood, may be used for the purpose of producing tetanus in mice. Inflammatory exudations containing large numbers of leucocytes appear to produce the tetanic symptoms even more readily than does the blood itself, and Metchnikoff suggests that in these insusceptible fowls the tetanus toxin is stored up in the leucocytes, and that the tetanus toxin, being taken up by these cells, is prevented from getting to the nerve-cells. Moreover, if the temperature of the fowl be lowered considerably, a condition under which the activity of the leucocytes is markedly diminished, the susceptibility of the fowl to tetanus becomes greatly increased. Again, as Roux and Borrel have pointed out, it is a comparatively easy matter to produce tetanus in the fowl by injecting the poison directly into the brain, so that when the fowl exhibits its remarkable resisting power it may be accepted that the poison never comes in contact with the nerve-cells; it is fixed and rendered innocuous, whilst circulating in the vessels and tissues of the organism, before it can get to the brain. Unlike the poison produced by many other organisms, that of the tetanus bacillus seems to produce much the same results whether it be injected subcutaneously into the thorax or abdomen, or into the veins. The tetanus bacillus appears seldom to attack an animal from the alimentary canal.

In tetanus experimentally produced the spasms are first observed in the muscles near the site of inoculation; but ultimately the contractions may become general. After intraperitoneal or intravenous injection, however, there is usually a general infection from the outset. In many cases the changes at the seat of inoculation may be so slight as to be overlooked unless carefully searched for. This point is of special importance, as

many cases of tetanus are said to be idiopathic; in these, however, it is probable that the initial local damage has escaped observation. Even in experimental tetanus there is, as a rule, only slight infiltration at the seat of inoculation. This *absence of local manifestation* appears to indicate that the tissues at this point are incapable of reacting, and that the poison has been rapidly absorbed from the seat of introduction. It is only when mixed cultures are injected, or cultures mixed with foreign bodies, such as pus, pieces of tissue from a wound, soil, etc., that a local suppuration takes place.

The tetanus bacillus (or its spores) when introduced alone does not set up suppuration. Vaillard points out that in one of his animal experiments, in which he had introduced spores under the skin, the wound healed at once. For some time no symptoms of tetanus arose; but when, later, the wounded limb was irritated the spores became active and an attack of tetanus was the result. In those cases where tetanus is propagated after the wound has been treated antiseptically, it must be assumed that spores which have not been killed by the antiseptic agents have remained latent in the healing tissues for some time. Later they have developed into bacilli, have commenced the manufacture of their toxins, and have then induced an attack of tetanus.

Vaillard and Rouget, and Vincent state that spores of the tetanus bacillus from which all traces of poison have been removed by careful washing, when inoculated alone into an animal, are incapable of setting up tetanus. Klipstein, on the other hand, maintains that this washing of the spores injures them so seriously that they certainly lose a great part of their infective property, but that this infective power is never entirely lost. Vaillard and Rouget, however, are satisfied that their own observations are correct. It is certainly true that in many cases pure cultures of tetanus bacillus fail to set up a tetanic infection; but this may be due to the activity of the tissues and fluids, as equally well-marked failures to infect may be observed in the case of the infective agents of other diseases.

Speaking generally, tetanus, experimentally produced, follows so distinctive and regular a course that it may be divided into three stages (Knud Faber)—(*a*) *the incubation-period*, (*b*) *the stage in which local spasms are developed, and* (*c*) *the stage in which general tetanic convulsions occur.* In certain of the smaller and very susceptible animals the incubation-period extends over a comparatively short time. For instance, in mice inoculated with pure broth cultures of the tetanus bacillus, the incubation-period may be as short as five or six hours, though it may be as long as from twenty-four to forty-eight hours. When earth is used the incubation-period is somewhat longer, and is usually put down at from two to three days. In the guinea-pig the incubation-period is slightly longer, being usually from one to two days. There is some difference of opinion as to the period of incubation in the rabbit. Knud Faber describes the incubation-period in this animal as being from twenty-four to forty-eight hours; other observers place it at from eight to fourteen days. There can

be no doubt that the period of incubation varies considerably in rabbits according to the dose administered and the size and age of the animal experimented upon. Trismus, which is a marked feature in the rabbit when the incubation-period is short, is seldom observed in the mouse or in the guinea-pig. After the injection of very virulent cultures general tetanic convulsions, such as are seen in the mouse, are never observed in the rabbit. Knud Faber observed that there is no gradual transition from the local spasm to the general tetanic convulsions, but that we have a sharp line of demarcation between the two; the general muscular spasm beginning as an entirely new phenomenon is perfectly distinct from the local symptoms. The disease in the rabbit is specially interesting, because in it the disease manifests itself much as it does in the human subject, both as regards the non-fatal form of the disease, in which merely local spasms are developed, and the malignant type, which begins with local spasms, and passes on to trismus and stiffening of the neck; when an intravenous injection of the virus is made a general tetanic condition corresponding in almost every detail to that seen in the human subject may be produced. In the human subject the period of incubation is of course somewhat longer, from one to twenty-two days: von Hacker describes a case in which the incubation-period was between five and six weeks.

The tetanus bacillus is localised entirely in the region of the seat of inoculation: it is never found in the blood or fluids of the viscera, or in distant tissues; and no changes are demonstrable in the organs other than those of the central nervous system. Hence the failure of earlier experimenters to produce the disease by the injection of blood from tetanic patients. In tetanus, an essentially toxic process, the poison is absorbed from the seat of inoculation, where it may have been originally introduced in sufficiently large quantities to bring about the characteristic tetanic symptoms in a very short time; or where it may have been manufactured by the tetanus organisms so favourably situated that they can develop a sufficient quantity of their products to set up toxic symptoms: the bacilli, then, are distinctly localised, but the poison may be widely diffused. Kitasato and Knud Faber, working independently, pointed out that the whole of the phenomena of a fatal attack of tetanus may be induced by the injection of the poison quite apart from the bacilli by which it was formed. Kitasato inoculated mice at the root of the tail with cultures of the bacillus; and after a half, one, and one and a half hours respectively, he cut freely around the inoculation wound and carefully cauterised it, thus removing all the bacilli that he had introduced. He found, however, that only the animals in which the parts were removed at the first of these intervals escaped an attack of tetanus; from this he argued that the poison formed by the bacilli, and not the bacilli themselves, is the essential factor of the disease in experimental tetanus. Vaillard and Vincent, who repeated these experiments, came to a similar conclusion.

Most cases of *accidental traumatic tetanus* differ materially from

cases experimentally produced, in that other organisms and foreign bodies are frequently introduced with the specific bacillus; suppuration is set up, and under these conditions the tetanus bacillus appears to have peculiar opportunities of developing its poison. It is sometimes stated that the tetano-toxin is produced for a time only, and that the development of the bacillus is soon arrested, even in cases that ultimately succumb to the disease; but Roux and Vaillard maintain that this is not true, and that before a case of tetanus can be treated with any degree of success the infective focus must be freely removed so that the supply of toxin may be cut short. So long as bacilli continue to multiply in the wound, they are probably producing poison; and therefore every attempt should be made to limit their increase. The point of entrance of tetanus virus is usually a wound which may be on the outer surface; in the uterus after childbirth, or in the severed cord of the new-born child. Patients, as we have seen, are usually affected when working amongst horses, or when wounded while following agricultural pursuits. It is maintained, indeed, that the horse being the natural host of the tetanus bacillus, this micro-organism is found in and spread with the dung of this animal.

The tetanus poison resembles the enzymes in many respects; it is destroyed at a temperature of 65° C. in about five minutes; even if maintained at the temperature of the body for any length of time it may gradually become weakened. When kept on ice, and protected from the action of light, it retains its poisonous properties unchanged for months. By the addition of toluol, of 0·5 per cent of carbolic acid, or of an equal volume of glycerin, it may likewise be preserved for some time. It is not affected by drying at ordinary temperatures; but owing to its great instability in the presence of most of the ordinary chemical reagents, it is an exceedingly difficult matter to obtain this poison as a pure substance. Brieger first isolated three substances—tetanin, tetano-toxin, and spasmo-toxin—by means of which tetanic symptoms and in some instances death could be induced in animals; but it is evident that, as these substances had to be given in such enormous doses, none of them can be the essential poison of tetanus which acts in the extremely minute doses described on p. 1047. Kitasato and Weyl obtained two ptomaines, one very slightly toxic, which they named chlorhydrate of tetanin, the other a tetano-toxin compound which produced paralytic symptoms. Brieger and Fränkel then described a proteid poison which they obtained from cultures of the tetanus bacillus, and named tox-albumin; they separated it by saturating with alcohol the fluid in which the organism had grown, whereupon a precipitate having an extremely powerful action is thrown down. It has been suggested, however, that this albuminous precipitate simply serves as a kind of net-work in which the essential toxic substance is entangled. Knud Faber, Tizzoni and Cattani, and Vaillard and Vincent affirmed that this poison is probably of the nature of a diastase. Brieger, and Kitasato and Weyl then succeeded in obtaining an extremely virulent poison which does not

give the reaction for albumins. It consists of yellow, transparent flakes readily soluble in water; it is not destroyed by drying, nor in the dried state by absolute alcohol, chloroform, or anhydrous ether; it is very readily decomposed by acids or alkalis, by sulphuretted hydrogen, and by high temperatures: in these features it resembles tetanus poison in its original solution. Its toxic power is represented as being 500 times as great as that of atropine; and 120 to 400 times as great as that of strychnine. Although so much is known of the physiological action of this substance, very little light has been thrown on its chemical composition. Brieger and Cohn maintain that since tetanus bacilli have the power of producing the poison in non-albuminous media the poison must be looked upon as probably non-proteid. It must be remembered in this connexion, however, that the protoplasm of many bacteria has the power of building up proteid substances out of non-proteid foods. The virulence of the poison and the nature of its action upon animals both appear to indicate that it is of the nature of an enzyme or a diastase.

Tetanus in man is accompanied by the same series of processes that have been induced in animals in experimental tetanus. As we have already seen, it occurs sometimes in patients suffering from suppurating wounds, such suppuration being the result of a mixed infection. In man as in animals it is found that the bacilli never pass from the immediate neighbourhood of the seat of the original lesion, which, then, must be looked upon as merely the local manufactory of the poison. The toxic products of the tetanus bacillus can, however, be demonstrated in the blood of the general circulation; and tetanic symptoms have been induced in mice by injecting the serum of the blood from a tetanic patient; again, toxic products have been obtained from the liver, spleen, and spinal cord of patients who had succumbed to tetanus. These toxic products, obtained by throwing down an alcoholic precipitate and dissolving it in water, when injected into small animals have set up all the symptoms of tetanus. The tetanic poison appears to be excreted in the urine and also in the milk.

Bacteriological Diagnosis.—A drop of the pus containing the "drumstick" organisms or other suspected material is inoculated into a subcutaneous pocket just above the root of the tail of a mouse; if the material contain tetanus bacilli the animal usually succumbs in the course of a few days. Or a small amount of pus taken from the seat of inoculation may be used for inoculating agar-agar slope tubes, the growth from which may afterward be treated by Kitasato's method. Or, again, the suspected material may be inoculated into bouillon which is incubated in an atmosphere of hydrogen for three to five days; this broth, with the organisms growing in it, is then placed in a water-bath kept at a temperature of 80° C.; here it is left for one hour, after which a fresh anaerobic bouillon culture is made; this process is repeated until pure cultures of the tetanus bacillus are obtained.

Effect of Tetanic Poison on the Nervous System.—Since muscular spasms are such a constant and striking feature in poisoning due

to the action of the tetanus bacillus, and since, too, the dosage of the poison can be pretty accurately measured, and the living bacilli eliminated from the equation, much experimental work has been done on the etiology and pathology of tetanus; though many points still remain to be cleared up. As regards the pathogenesis of the disease, the researches of Pasteur on rabies led earlier investigators to suppose that tetanus was due to the presence and action of some virus which they assumed must be formed in the nervous system, especially in the spinal cord; and that the violent nervous symptoms were induced by the action of this virus. Knud Faber made a number of inoculation experiments with material taken from the nerve-centres, but, like the experiments of those whose work in this direction had preceded his own, they entirely failed; as did also his attempts to obtain any bacilli from the tissues of the central nervous system even in marked cases of tetanus. He concluded, therefore, that the virus could not be formed in the central nervous system, as it was evident that the poison could not be formed without the intervention of the tetanus bacilli. Following up Brieger's intoxication hypothesis, Knud Faber was able to show that a pure culture of the tetanus bacillus produces during its growth a poison or group of poisons, which, when isolated entirely from the bacilli, is still capable of setting up characteristic tetanic symptoms. This was not an entirely new observation, but it is to Knud Faber that we owe the first demonstration that the poison only acts after a certain period of incubation, this period depending upon the amount of poison introduced. He also pointed out that it has many of the characteristics of the diastase or enzyme group, and that we should argue from the period of incubation that it requires time in which to set up certain fermentative or diastatic changes in the fluids or tissues of the body. He also showed that five minutes' heating at a temperature of 65° C. is sufficient to destroy the activity of this poisonous substance; moreover, as was afterwards pointed out by Vaillard and Vincent, the poison can be separated from a filtered fluid by the method used for separating diastase, that is, along with a precipitate obtained from a solution of calcium hydrate on the addition of weak phosphoric acid.

When this poison is introduced into the subcutaneous tissues it sets up local spasmodic contractions; when injected intravenously general contractions occur at the very outset after the incubation-period; the incubation-period is, however, well marked in both cases. Tizzoni and Vaillard, working independently, cut through the nerves of a limb before inoculating the animal with tetanus virus. This limb remained flaccid when all the rest of the muscles had been thrown into a state of spasm. Buschke, adopting a different method, curarised a tetanised frog, and found that the tetanic contractions were immediately abolished. It may, therefore, be concluded that the poison does not act directly either on the muscles themselves or on the peripheral nerves. This observer found also that the tetanic state remains even after removal of the brain of the frog, and that tetanus is not set up on the direct application of tetanus

virus to the cortex of the cerebrum. Again, progressive destruction of the spinal cord caused the tetanic symptoms to disappear from the part corresponding to the region of the spinal cord removed from the tetanised animal. Consequently, he argued, the action of the poison seems to be localised in the spinal cord just as in the cases of strychnine and brucine poisoning pointed out by Simpson.

Gumprecht, from a series of experiments on frogs—in one series of which he used strychnine, and in another filtered bouillon cultures of tetanus bacilli—came to the conclusion that the general spasms produced by both substances must be referred to a toxic affection of the central nervous system, causing increased reflex excitability of the spinal cord. The local tetanic spasms, although more difficult to explain, he considers result from excitation of the nerve-centres, this excitation taking place at a very early period after the introduction of a large dose of the poison, which, as pointed out by Behring, and Vaillard and Vincent, may travel in an almost incredibly short space of time from the seat of inoculation throughout the body. Gumprecht maintains, too, that the local spasms around the point of inoculation do not arise reflexly by irritation of the peripheral ends of the sensory nerves; for when the whole of the sensory nerve-roots of a limb were cut, and the limb completely anæsthetised, tetanic spasms still made their appearance. He found that the motor terminal plates and the muscle itself were unaltered by the tetanus poison, as muscles tetanised for a long period still gave perfectly normal contraction curves, whilst there was complete absence of the reaction of degeneration from such muscles. Gumprecht considers that the local symptoms are most readily explained on the assumption that the poison travels along the nerves, and thus enters the spinal cord at certain definite points, corresponding, of course, to the point of inoculation, where it is more or less localised for some time after its arrival at the cord. In this way he explains the extension of the tetanic symptoms to those muscles which have their nerve-centres in the immediate neighbourhood of those nerves which pass from the site of inoculation; it is found also, and probably for the same reason, that the inoculated half of the body of the experimented animal is usually affected earlier and more profoundly than the opposite side.

Goldscheider agrees with Gumprecht that after subcutaneous injection of the tetanus bacillus, or tetanus poison, the outbreak of general tetanus is preceded by the contraction of those muscles which lie next to the region of inoculation; and he believes that this is due to the action of the tetanus poison on the central nerve-cells, in consequence of which they assume an increased and ever-increasing excitability, the change taking place gradually, but going on continuously so long as there is any absorption of the poison from the wound. He maintains, too, that the poison is conveyed to the nerve-centres by the blood-vessels and lymphatics of the nerve-trunks, and that it there acts on the ganglion-cells, increasing their excitability and gradually affecting a larger and larger area; but he believes that in addition there is a general diffusion

of the poison by means of the blood and lymph; to this the general spasms are to be attributed.

Tiberti, in a recent article, draws attention to the following important points, most of which he has demonstrated very clearly. The greater portion of tetanus toxin injected subcutaneously passes into the lymph-vessels and thence into the blood, a small portion is absorbed by the nerve-endings and transmitted by the nerves to the nerve-centres. This transmission is not by the lymph-channels of the nerves, but along the plasma of the axis-cylinder, in a cellulopetal direction; this is probably due to the attractive action of the nerve-cells. When tetanus toxin is injected into a muscle it diffuses in the serous fluid, bathing the muscle, and, after absorption by the nerve-endings, is conducted by the nerves to the nerve-centres. Minimal doses of toxin, when injected directly into the nerve-parenchyma, induce severe tetanic phenomena, but the same doses injected subcutaneously have no effect. An injection of tetanus antitoxin into a nerve-trunk inhibits the passage to the nerve-centres of a succeeding injection of toxin into the muscles supplied by this nerve, and no muscular phenomena of any kind are exhibited in these muscles. Toxin injected into a nerve is carried to the nerve-centre by the nerve-substance itself. Subcutaneous injection of toxin induces no tetanic phenomenon in muscles, the nerve-trunk to which is severed. When toxin is injected directly into the substance of the spinal cord the incubation-period is considerably shortened and a characteristic clinical picture results (*Tetanus dolorosus*). When toxin is injected into the circulation all the muscles are seized with tetanic contractions simultaneously, and the so-called *local tetanus*, observed after subcutaneous injection or into the nerve parenchyma, is absent. A larger dose also is necessary to induce symptoms. The toxin passes quickly into the lymph, but cannot be demonstrated in the cerebrospinal fluid. It is exceedingly interesting to note that fowls which manifest such a marked resistance to the action of strychnine, exhibit a similar resistance to the action of the tetanus poison, large doses of which may be introduced subcutaneously with very slight effect indeed. It will be remembered that both these poisons induce great irritability of the central nervous system; especially in the case of animals susceptible to their action. In fowls it is difficult to induce this irritable condition except when the poison is introduced directly into the nerve-substance. Brunner observed that spasms in the facial muscles are set up both by subcutaneous inoculation in the face, and by subdural inoculation in the opposite half of the brain. Kübler in a note on this observation points out that tetanus in man does not follow the course above described. In man local symptoms in the vicinity of the site of infection are seldom manifested; trismus is as a rule the first sign, the pharyngeal muscles are then affected, and gradually in turn the muscles of the trunk and the lower limbs. This criticism, however, does not appear to be very forcible. In cases of tetanus in the human being, except in those which run their course with great rapidity, the formation and diffusion of the poisonous products of the tetanus

bacillus go on much more slowly than in animals under experiment; and it appears quite probable that, as diffusion takes place so slowly, a certain time is required for the poison to accumulate to a degree sufficient to give rise to manifest symptoms of nervous irritation. If this be the case, those muscles which are least under control, and which under emotion are most readily stimulated, would be first attacked, and this appears to be the order in which they are attacked in tetanus—those which are least under control of the will, and in which the inhibitory mechanism is least strongly developed, are first attacked.

There appears to be not the slightest doubt that in certain animals most marked changes are induced in the large cells of the anterior horn of the spinal cord, as the result of the action of the tetanus toxin. There appears to be less unanimity of opinion as to the changes that take place in the cornual cells in the human subject, and even in the horse, as also in those in the brain, especially in the motor areas. Nissl, Goldscheider, and Flatau, Marinesco, Babes, and Mr. Foulerton and Dr. Campbell Thomson all describe the changes in the cells of the spinal cord of small animals, whilst the latter observers agree with those pathologists who maintain that not only the cornual cells but the cortical cells of the brain of the human subject undergo marked changes during the course of an attack of tetanus. There appears to be a distinct loss of the chromatic granules throughout the whole or a part of these cells, this being especially marked in the neighbourhood of the axis-cylinder process, though this is by no means constant, and may be localised in any part of the cell; this is especially the case in the brain-cells. Such a condition has not been seen in the cells of animals or human beings affected by the toxic products of other micro-organisms. Mr. Foulerton and Dr. Campbell Thomson conclude:—"1. That certain definite histological changes are produced in the motor nerve-cells of the cerebral cortex by the action of tetanus toxin. 2. That with efficient doses of the toxin such changes are of constant occurrence, since they were manifest in each of fourteen experimental animals. 3. That whilst the occurrence of a change of some sort is constant, the exact histological appearances produced vary with differences in the accompanying factors relating to time and dose."

Following up Pasteur's, and Salmon and Smith's experiments on the production of immunity, and on the antitoxic power of the serum of immunised animals in the treatment of a particular specific septicæmia, certain experiments were made on the establishment of **immunity from tetanus.** For a long time these experiments bore little fruit. At length Behring and Kitasato succeeded in producing a transient immunity in rabbits by inoculating them with the filtrate from a culture of the tetanus bacillus, and then injecting at the same point a small quantity—3 c.c. of a 1 per cent solution—of terchloride of iodine for five days at intervals of twenty-four hours. On injecting 0·2 c.c. of the blood of a rabbit thus immunised into a mouse (an animal in which they had previously failed to obtain any immunity), it was found to be protected in a

certain degree against the disease that should, under ordinary conditions, have been set up when the virus was inoculated subcutaneously. This same treatment also proved efficacious when carried out on mice that had already been infected with the tetanus bacillus, and even after symptoms had appeared after such infection. It was found, moreover, that several hundred times the lethal dose of a virulent culture, if first mixed with a certain quantity of serum from an immunised animal, might be injected without producing any morbid symptoms. The following year Tizzoni and Cattani confirmed Behring and Kitasato's observations on the specific antitoxic power of blood-serum taken from immunised animals. Roux and Vaillard obtained similar results by taking four to five weeks' old bouillon cultures of the tetanus bacillus, passing them through a Chamberland filter to keep back the bodies of the bacilli, and then injecting the resulting filtrate, which contained the soluble poison, mixed with weak iodine solution, using less and less iodine at each successive injection until, as the animals became more and more poison-proof, considerable quantities of the culture unmixed with any of the iodine solution could be tolerated. Once attained, they found that this immunity may be easily kept up by fortnightly injections; if the animal be left untreated for a fortnight or three weeks the antitoxic power of the serum begins to diminish, though it may not be entirely lost for a very long time—a couple of years. When tetanus poison is injected it is absorbed rapidly, and antitoxic substance almost as rapidly makes its appearance in the blood. Roux states that thirty-five minutes after the injection of toxin into the abdominal cavity of a rabbit antitoxin may be found in the blood drawn from the lateral vein of the ear.

Susceptible animals, such as the mouse, rabbit, horse, and sheep, may also be immunised; but in their case the process requires to be much more carefully carried on, and is necessarily much more tedious and prolonged. Behring, after long-continued experiment, found that he was able to obtain the necessary immunity by injecting filtered bouillon cultures of the tetanus bacillus, to which had been added a solution of iodine trichloride, first in the proportion of 0·25 per cent, then of 0·2 per cent, then of 0.15 per cent, until, finally, unaltered filtrates were used, first in small doses at intervals of three to five days, then in constantly increasing doses at intervals of eight days. In place of this method Vaillard produced a similar immunity by injecting for a few days a filtrate previously heated to 60° C., then a series heated to 55° C., and finally to 50° C. Gram's solution and lactic acid have also been used for the purpose of attenuating the strength of the tetanus poison and the activity of the bacilli.

Behring has shown that mice which had been poisoned with fatal doses could be cured even after the appearance of the first tetanic symptoms, in some cases five hours after. The animals survived, but only after a prolonged illness; and if he allowed a period of twelve hours to intervene between the first appearance of the tetanic symptoms and the commencement of treatment, the cases almost invariably had a

fatal termination. He worked this out so accurately that he found if the animal were treated before inoculation with the tetanus bacillus it required for its protection only one-hundredth part of the dose that was necessary if the treatment was not commenced until a quarter of an hour after infection.

Tetanus was the first disease of this class in which careful investigation led to results which, though comparatively unimportant in themselves, paved the way for the more important serum treatment of diphtheria. In tetanus definite symptoms could be noted in animals in which the experimental infection succeeded; here also the toxic products of the bacillus could be readily separated, and the dose required to produce definite symptoms accurately determined. Ehrlich and Tizzoni and Cattani experimenting with the rat and rabbit and treating them with the blood-serum of animals which had been rendered refractory to tetanus, found that they were always able to obtain a cure if the injections were commenced as soon as the first symptoms manifested themselves. When the local symptoms were established, or beginning to disappear, the results they obtained by the serum treatment were less certain; while in those cases in which tetanus was already becoming generalised success never followed this treatment. Ehrlich's theory of immunity is based upon the fact that in an animal immune from a specific infective or toxic disease the tissues are poison-proof; that is, the poison (the tetanus poison, in this instance) can no longer exercise upon the immune animal or its tissues any deleterious effects. As is well known, some animals are less susceptible to the action of certain specific infective diseases than are others; and in the case of tetanus it has been found that comparatively insusceptible animals —such as the dog and the fowl—may be rendered less and less susceptible, by the injection of gradually increasing doses of the specific poison. It is then found that their serum (although previously it had no antitoxic action when injected into another animal), in cattle the milk, and in the fowl the yolk of the egg, have, as the result of this treatment, acquired considerable immunising power; and this serum (or these other substances), on being artificially introduced by injection into susceptible animals, acts so rapidly upon their tissues that they in turn are rendered comparatively insusceptible. This power, as we have already seen, is extremely well marked if the serum be introduced at the same time or shortly after the tetanus poison; but its power of doing good diminishes more and more rapidly as the tetanus poison obtains a longer start. In the light of the comparatively unsuccessful use of antitoxic serum in tetanus in the human subject, it is interesting to note that the quantity of serum required for a successful result after local symptoms have commenced is at least from one to two thousand times greater than that required to confer an antecedent immunity. This remarkable fact should be borne in mind in determining the efficacy of the antitoxic serum method of treatment. Further, it is calculated that a dose of serum at least 150 times as great as the above curative

dose must be employed if any success is to be obtained when the local symptoms have reached their height.

The curative action of the serum is said to depend entirely on the proportion of antitoxin which it contains, so that, if the proportion of antitoxin in the serum is known, the dose can be accurately calculated. Antitoxin is stated by Roux and Vaillard to be an enzyme, which it resembles in many respects; its comparative stability, however, is different, for it will even stand a temperature of 70° C. without undergoing any appreciable alteration. Tetanus antitoxin may be kept indefinitely in the form of scales obtained by evaporating the blood-serum at a low temperature *in vacuo.* At the moment of using it is dissolved in six times its weight of sterilised distilled water.

Tizzoni and Cattani found that the antitoxic substance, when precipitated from the serum by alcohol, does not lose its strength; they urge, therefore, that the alcoholic precipitate, which is non-dialysable, may be substituted for the serum itself. Assuming that the experiments made on the rabbit can be applied to man, they calculate that it would be necessary to give 0·7 c.c. of the serum, or 0·06 gramme of its alcoholic precipitate, at the outbreak of the first symptoms of tetanus; whilst at a more advanced period it might be necessary to inject 210 c.c. of serum, or 12 grammes of its precipitate. This is an exceedingly large quantity to inject subcutaneously, yet in medical practice even this quantity has failed to give satisfactory results. In fact, these observers were unable to obtain a much greater percentage of recoveries by this method than had previously been obtained in cases treated without serum. They were the first to differ from Behring who maintained that the antitoxin, or the antitoxic serum, directly destroys or antagonises the toxin formed by the tetanus bacillus; they ascribe to it a power of enabling the tissue-cells to continue their work in the presence of larger doses of poison. Roux and Vaillard also maintain that Behring's theory is untenable, namely, that each injection of toxin diminishes the immunising power of serum; and that, if too large or too frequent doses be injected, the antitoxic property of the blood may disappear for a space and the blood actually become toxic. Were the antitoxic serum merely a neutraliser of the toxin, the horse under these conditions should manifest the symptoms of tetanus. This, however, is not the case, and since the antitoxin has disappeared, the immunity of the animal must depend upon something else, a something which appears to be the habituation of the tissue-cells to the presence of the toxin; the cells can go on doing their work under the gradually acquired new conditions, and no tetanus is set up. This result is best obtained by the injection (into a horse) of 200 or 300 c.c. of the toxin, after which dose the animal supplies a sufficiently potent serum.

Antitoxic serum confers an immunity which for a time is perfect, but is more transient than the immunity brought about by the injection of toxins or of the specific organism (when it may last for as long a period as a couple of years). In most cases it is lost at the end of six or eight

weeks. Immunity certainly continues as long as any antitoxin remains in the blood. As would be expected, therefore, the antitoxic property of blood disappears long before the immunity of the animal from the disease is lost. This immunity can only be obtained with the toxins when they are injected repeatedly and in large quantities. It must be remembered in this connexion that the antitoxic substance is constantly being excreted by the kidneys, by the mammary, and probably by other glands; but a certain quantity undoubtedly remains for some time after the injections have been discontinued. Ehrlich believes that the hereditary transmission of immunity is due to the large quantities of antitoxin excreted in the milk: if this opinion be correct the stability of the antitoxic substance is much greater than has generally been supposed. The practical importance of this assertion should not escape observation.

Although the antitoxin is so rapidly excreted by the glands, it has been observed that repeated blood lettings, if they be carried on during a short period, do not seem to lower the antitoxic power of the serum.

In man, as in animals, it is found that the shorter the incubation period—that is, the period intervening between the infection and the outbreak of the disease—the more severe the disease and the worse the prognosis. It is stated that of those cases in which the incubation period is under ten days, not more than 3 to 4·5 per cent recover; when the incubation period is from eleven to fifteen days, 25 per cent recover; in those cases in which the incubation period is still longer, about half the patients attacked throw off the disease. Different authors give somewhat different statistics, but these are the general results.

Statistical results of treatment with antitoxic serum.—Kanthack (1895), in a series of tables, including 54 cases that had been treated with antitoxic serum, gave the duration of the incubation period, date of the disease when treatment was begun, quantity of serum injected, the result and the duration of the illness. Of this series 20 or 37 per cent proved fatal. In 1896 and 1897 he collected 55 more cases, of which 23 or 42 per cent died. He arrived at the general conclusion that in most of these cases too little antitoxin was used, it was given much too late, and that in many of the cases that did recover the antitoxin had nothing to do with the improvement. The largest series of cases collected since those tabulated by Kanthack are one by Vallas, and a second by Moschcowitz. Vallas gives an analysis of 373 cases; of 141 in which the incubation period was less than ten days 80 or 57 per cent died; of 118 of which the incubation period was more than ten days 24 or 20 per cent died; and of 114 in which the incubation period was unknown 41 or 36 per cent died,—giving a total of 145 deaths or 39 per cent against 70 to 90 per cent under the old method of treatment. These results have been obtained in all probability (*a*) because of the more active antitoxin now in use; and (*b*) because the antitoxin has been injected at a much earlier period of the disease than was formerly the case. A series of smaller collections have been made, but we may take it that these are cases that have been more or less carefully

selected. Moschcowitz analyses 290 cases of tetanus that were treated by subcutaneous injection of antitoxin. Of these 117 died, giving a mortality of 40·33 per cent. Adopting Kanthack's method of statement it is found that of these cases 53 having an incubation period of less than seven days, 29 or 54 per cent died, whilst of other cases in which the period of incubation was longer and was known, there were 61 deaths out of 164 cases, a percentage of 35·36. Putting them in another form Moschcowitz states that "of 33 cases with a period of incubation of less than five days, 19 recovered and 14 died, 42·42 per cent; of 114 cases with a period of incubation of five to ten days, 52 recovered and 62 died, 54·38 per cent; of 64 cases with a period of incubation of ten to fifteen days, 52 recovered and 12 died, 18·75 per cent; of 24 cases with a period of incubation of over fifteen days, 20 recovered and 4 died, 20 per cent; of 55 cases with unknown or unreported period of incubation, 30 recovered and 25 died, 45·45 per cent." It is evident from all these statistics that the incubation period is a very important prognostic factor.

The immunising serum appears to have a special action on the same tissues as those attacked by the poison—probably on the ganglion-cells of the central nervous system; and the substance first in the field, be it toxin or antitoxin, appears to work at a very great advantage over that subsequently introduced. Moreover, the more directly and the more rapidly the antitoxin can be brought into contact with these same tissues, the greater will be the chance of recovery, and Roux and Borrel have introduced the intracerebral injection of antitoxin. Although the results in animals appear to be excellent, there seems to be considerable difference of opinion as to the propriety of making these intracerebral injections. It appears that injections even of small quantities of antitoxin into the cerebral substance is a somewhat dangerous method of procedure (unless carried out as below), as even when the greatest care is taken hæmorrhage supervenes in certain cases, meningitis in others, and abscess in others. Moreover, one surgeon states that of 20 cases in which subdural injections were made, 13 of the patients succumbed. Intracerebral injections in severe cases is recommended by Tavel, amongst others. He points out that this should be done by trephining and then injecting antitoxin directly into the anterior horn of the lateral ventricle, an operation, he maintains, that is attended with comparatively little danger.

The results obtained by intracerebral injections are as follows:—Of 48 cases injected, 25 died, a mortality percentage of 52·08. It appears to be very important in making these intracerebral injections that large doses should be thrown into the lateral ventricles at one injection, so that there may be no danger of secondary infection resulting from the passage of the needle through granulating tissue, which in certain cases may not be completely aseptic. Adopting Kanthack's classification as regards this method of treatment, we note that of 8 cases with an incubation period of less than seven days, 6 died, giving a mortality of 75 per cent. Of those with a longer period of incubation and in which the period was known,

15 died out of 34, giving a mortality of 44·1 per cent. Tavel and many surgeons strongly recommend an adjuvant intravenous injection in order to neutralise the circulating poison.

It should be noted that a much larger proportion of the recoveries from tetanus are published than of the fatalities, so that the above mortality percentage is probably somewhat too low. It is gathered from these tables that the cases of cure all belong to the chronic or benign (?) form of tetanus; whilst those cases that ended fatally invariably developed in less than fourteen days; in the majority of cases the duration of the disease did not exceed four or five days. In these cases, too, the period of incubation was comparatively brief.

Moschcowitz points out that the old method of treating symptoms is now no longer adequate; and that, accepting the fact that tetanus is a specific infective disease, we have certain definite indications as to the lines of treatment that should be adopted. The first of these is "to destroy the bacteria at the seat of infection, and thereby prevent a further production of toxins."

Subcutaneous and subdural injections of at least 50 c.c. of the antitoxin are recommended with the same object in view. There seems to be every reason that a prophylactic injection of tetanus antitoxin should be made in cases where wounds have been infected with material that may contain tetanus spores (horse manure, the soil in stables and fields where horses are kept, in the soil of ground over which cavalry have passed), as much smaller doses of antitoxin are necessary to prevent the disease than to cure it. In very severe cases there can be little doubt that we should take the risks of injecting into the anterior horn of the lateral ventricle, as well as of getting as much antitoxin as possible into the veins, the subcutaneous and the subdural tissues. It is now maintained that, as the result of better methods of treatment, and partly at any rate from the use of early and full doses of antitoxin, the mortality has fallen from 90 per cent to 40 per cent. It should be pointed out that even in those cases in which, through the use of large doses of antitoxic serum, the action of the toxin is brought to a standstill, these cells may, before the treatment commenced, have suffered very considerably; if so the recovery must necessarily be slow: in other cases the damage to the tissues may be so far advanced that recovery is impossible; for it must be borne in mind that the antitoxin can play no part in regenerating structures already destroyed or impaired. Its power appears to be, if used sufficiently early, to fortify the nerve-cells against the action of the poison, allowing them to carry on their work unchanged in the presence of what, under ordinary conditions, would lead to their complete disorganisation. It should be noted in this connexion, too, that the symptoms of spasm and irritability are considerably increased for some short time after the administration of the dose of serum, as though a contest for the mastery were actually taking place in the central nerve-cells. The more marked this feature the more prolonged is the process of recovery. This indicates, apparently, that considerable

disorganisation of the cells has taken place before the antitoxic serum has had time to act.

While on this point it may be well to indicate the reason for the difference that undoubtedly exists between the results obtained by the antitoxic serum treatment in tetanus, and by the similar method of treatment in diphtheria. In both cases there is a manufactory of the poison on or near the surface of the body. In both cases there is an absorption of this poison into the body, and in both cases the nervous and muscular systems are specially attacked by the poison. But in the case of diphtheria our attention is called to the manufactory of the poison at a very early stage of the disease; for it usually occurs in some part of the throat, where it gives rise to considerable discomfort: moreover, from the nature of the tissues in this region a false membrane is usually formed at a very early stage. Attention is therefore drawn to the local poison manufactory almost as soon as it begins to discharge its poisons into the system, and the serum may be utilised to antagonise the poison before it has had time to injure the nerve-cells, nerves, and muscles. It is interesting to note, too, that in a large number of cases of diphtheric paralysis, the diphtheria has been said to be slight; that is, the local manifestations of the disease have not attracted attention, and the process has been allowed to go on so long that the poison, though perhaps small in amount, has been allowed to act for a considerable length of time, and thus to bring about paralysis. In tetanus, on the other hand, the local wound by which the poison is absorbed is for a long time looked upon merely as a wound, a suppurating one, perhaps, but not a manufactory of the tetanus poison; consequently nothing is known of the tetanus until the poison has had time to exert its evil influence on the nervous system: and by the time we find out that the patient is suffering from tetanus the disease is so far advanced that any chance of treating it successfully by means of antitoxic serum is reduced to a minimum (*vide* p. 1074).

German Sims Woodhead.

Symptoms.—The chief symptom and feature of tetanus is the occurrence, and recurrence at varying intervals, of *spasms* of greater or less severity in the voluntary muscles. These spasms are superadded to a state of persistent tension of the muscles which, however, like the spasms, is commonly relaxed during sleep. They sometimes commence in the neighbourhood of the wound and spread to other parts of the body. It was so in a case of gunshot wound of the thigh, in a case of wound in the perineum by a pitchfork, and in the case of a wound in the face by the lash of a whip, all of which I saw. In another case the spasms in the injured part (the thigh) continued after those in the rest of the body had ceased under the influence of chloroform. In all these the affection was severe, and proved fatal. In inoculated animals the earliest tetanic symptoms commence in the muscles adjacent to the wound, and, later, become general (69). But more commonly in man the tension and spasms are first observed in the neck, giving the sensation of ordinary stiff neck

from cold. This is quickly followed by tension and spasms of the muscles of the jaw, causing more or less inability to open the mouth or protrude the tongue, the tip of which is pressed between the teeth in the attempt to show it, and the tongue is often wounded by the sudden closure and snapping together of the teeth. The effort to put out the tongue causes spasm of the facial muscles, giving that peculiar strained expression or grin designated the *risus sardonicus.* Often on asking a patient to show the tongue have I been startled by the unexpected manifestation of this fatal omen in cases of wounds which otherwise seemed to be doing well. This trismus, then, is almost invariably present in the advanced disease, in the more acute and graver cases it is often the first manifestation of the disease, but in less severe cases local pains and spasms may be the initial symptoms. In every case of tetanus the contraction of the masseter muscle is so marked that the rigid border may be felt quite distinctly through the cheek. Coincident with these early symptoms, or soon after, the front of the abdomen is felt to be firm or hard from contraction of the abdominal muscles. There may also be a sense of oppression or pain about the precordia, penetrating to the spine; this feeling of oppression is attributed to tension of the diaphragm, though it may be observed that the tension and spasm of the muscles in this stage are not commonly attended with pain. Soon the spasms extend to the other muscles of the trunk and to the muscles of the limbs, and, in some instances, are so severe as to cause rupture of their fibres; this event has occurred in the *rectus abdominis* and *psoas magnus.* Indeed, a case is quoted by Curling from Desportes in which both thigh-bones were broken by the force of the contracting muscles, and another in which the second cervical vertebra was dislocated. As a result of the contraction of the muscles of the neck the patient finds it difficult or impossible to touch the chest with the chin. The spasms usually affect the voluntary muscles in all parts about equally, those of the fingers, however, least; and the pain attendant on them varies. I do not think the pain is generally so severe as is commonly stated, and it rarely equals that attendant on common "cramp." In some cases it is sufficient to cause the patient to cry out, but often even boys do not give this or any indication of great suffering; the condition is rather that of forced and distressful straining, which is often very exhausting. When the spasm ceases the patient is worn out, subsides into quietude, and perhaps into sleep. The pain is chiefly felt along the back: and the dominating power, with perhaps more excited contraction, of the dorsal and lumbar muscles, as compared with the muscles in front of the body, causes some arching of the trunk backwards; to this the term *opisthotonos* has been given. I have not seen this condition in the marked form occasionally described, nor have I seen the bending in the opposite direction called *emprosthotonos,* nor that to one side called *pleurosthotonos.* The spasms arise spontaneously, sometimes waking the patient from sleep. They may be excited by any slight cause which disturbs the patient, and are often induced by the effort to swallow the viscid saliva which accumulates in the mouth, is pressed out between the lips, and is a

source of much distress. The muscles of the glottis are not uncommonly affected, causing noisy, difficult inspiration, or stopping of the breathing; and death may thus result. Not unfrequently, when the sufferer has become worn out, a severe spasm, compressing the thorax, suspending respiration, and embarrassing the heart's action, squeezes life out, as it were, and leaves no power to recover it. In acute cases death usually occurs about the third day. In less severe cases life may be prolonged for a fortnight or three weeks, or even more. These prolonged cases afford the best prospect of recovery. On the whole, the disease is most severe and most quickly fatal when it commences soon after the injury, and when the injury is most severe. The brain commonly shows no sign of being affected, the intellect remaining clear to the last, though *delirium* has ensued in a few cases. The pulse is quickened during the seizures, but in the intervals between them the *pulse* and the *respiration* may be natural in rate. The *iris* commonly responds to light, and variations which have been observed in the pupil—contraction or dilatation—were probably due to the drugs administered. The *temperature* varies, and commonly rises during the paroxysms. In a case in Addenbrooke's Hospital, in which tetanus followed a wound in the perineum by a pitchfork, the temperature was 99·5° F. on the third day of the attack (the day of admission), on the fourth day it was 100°, and on the fifth day, during a severe and prolonged spasm which terminated the case, it rose to 106·4°. In a lad, who recovered, the temperature was on several occasions 104°-105°, and at these times the spasms were severe and frequent, and the breathing hurried. A similar remarkable or even greater rise of the thermometer (up to 110°) has been observed in other cases, and the high temperature probably contributed to bring life to an end. The thermometer has also been observed to rise after death. In some instances, however, where death has been preceded by a longer period of exhaustion, a fall of temperature has preceded the fatal event.[1] In the case from a perineal wound just mentioned the catheter was required on the third day, though only seven ounces of *urine* were withdrawn. Subsequently the urine was passed voluntarily, though with pain. The amount of urine varies, in some cases it is more, in some less than normal. It has been found to contain the tetanus toxin in considerable quantity, and injection of the urine into animals has induced fatal tetanus. This passage of toxin with the urine has given rise to the idea that an increase of diuresis might assist in the elimination of the poisonous material from the system; I am not aware, however, that the idea has been carried into practice. The presence of the toxin does not cause any increase in the quantity of urine secreted. The amount of toxin in the urine has been observed to diminish after the injection of antitoxin.

As tetanus is not usually attended with fever, so the blood drawn

[1] The rise of temperature may be due to the increased muscular metabolism caused by the continuous and the spasmodic contractions, or to an excitation of the nervous heat-centres. This question is much discussed, and many examples given by Rose, "Ueber Starrkrampf," in the *Handbuch der Chirurgie*, von Pitha und Billroth, Band I. 2. Abteil.

does not present inflammatory characters. The appetite and digestion are good. The tongue is usually whitish and the perspiration excessive. In most instances there is marked and rapid wasting of the system and diminution of strength. This *wasting and exhaustion*, indeed—this rapid wearing out of the bodily powers—constitutes an important and grave feature in the malady, and one which directly or indirectly leads to the fatal result. It is proportionate to the acuteness of the attack, and seems to depend upon some deleterious influence of the toxic agent acting immediately upon the system. I say this because, though much increased by the recurring spasms, it goes on manifestly when these are mitigated or suspended. The spasms, in truth, are but a peripheral symptom of the disease, though they exert a depressing and exhausting influence upon the body.

The *involuntary muscles* do not appear to participate with those of the voluntary system in the disturbances caused by tetanus. The bowels are commonly inactive, the muscles of the alimentary canal give no indication of spasms, and purgatives act as usual. The bladder and heart are in like manner free. Some observers, as Dr. Parry, attach much importance to the state of the heart, and think that it is the organ which first loses vital power; there seems no sufficient reason for this view. The pulse does but vary with the state of the patient, rising during the paroxysms, falling again when they subside, and becoming weaker as the general strength fails; death ensues from general failure of strength or violent general spasm rather than from any special failure or spasm of the heart.

Many cases of so-called *spontaneous* and *idiopathic tetanus* have been recorded in which no wound or other local lesion could be discovered. Some of the most virulent cases of tetanus appear to be of this kind, but they are in all probability due to infection through wounds or scratches of the mucous membrane of the alimentary canal. These may take the form of an ulcer in the mouth, the pharynx, the alimentary canal (12), or some other undetected part. Possibly the proportion of recoveries in the supposed idiopathic cases is attributable to the fact that the undetected local lesion is small in these cases, and the amount or virulence of the infection less. The attack has in many instances been attributed to cold or damp. A healthy-looking man, æt. 54, was admitted into Addenbrooke's Hospital, May 11, 1856, with the usual symptoms of tetanus well marked. They had commenced four days previously, with stiffness in the neck and jaws, after exposure to steam and cold winds in his occupation of boiling bones. It must be borne in mind, however, that this individual must have been exposed to scratches and bruises inflicted by the dirty bones. There was no apparent local lesion. The spasms were severe and general, and attended with difficulty of breathing, attributed in part to the firm closure of the lips. Still he was able to swallow in the intervals, though with some difficulty. Quinine, beef-tea, and wine were given in considerable quantities and frequently. Though thinner and weaker he held on without change for a week. After this he grew

worse. He could not sleep, yet morphine seemed to do him harm, causing increase of spasm. Chloral did better, and gave some repose. On the 26th he began evidently to improve, and he finally recovered, though it was long before he was free from the stiffness in the back, neck, and jaws.

The affection is said also to have occurred in *cases of contusion.* The following case, of which Mr. Charles Lucas, of Burwell, has kindly sent me the particulars, appears to belong to this class. A stalwart man, æt. 30, received a kick from a horse in the left thigh on March 9, 1883. On the 13th, when first seen, there was a hard, brawny swelling, very tender and painful, in the middle of the outer side of the thigh. No scratch or trace of wound was discoverable there or elsewhere. Fomentations and poultices were applied. In the night of the 24th his back and jaw became stiff, he was unable to open his mouth, and swallowing was difficult. Next day these symptoms had increased, and there were violent, painful spasms, with rigidity of the muscles of the face, neck, back, and abdomen; also pain about the region of the stomach, firm clenching of the jaws, and complete inability to swallow, the attempt to do so bringing on severe spasms. A free incision into the swelling of the thigh gave vent to a large quantity of fœtid greenish fluid, which was followed by almost immediate relief to the symptoms. On the following day, 26th, and on the 27th he could swallow gruel, and the stiffness and spasms had nearly subsided. On the 28th there was a complete recurrence of all the tetanic trouble, and a cessation of the discharge from the wound. The symptoms again ceased when the wound was freely reopened, and did not recur. The man completely recovered, though the convalescence was slow.

Diagnosis.—Tetanus may be distinguished from *hydrophobia* by the persistence of the muscular contraction in the intervals between the spasms, evinced by the closure of the jaws, by the hard sharp line along the margins of both masseter muscles. As Rose and others point out it is necessary to eliminate the possibility of inflammation and abscess or tumour setting up the same irritation and contraction of the masseter. In cases of true tetanus it is sometimes found that the lips are shot out or protruded by marked contraction of the orbicularis oris. The eyebrows may also be raised giving the patient a "scared" expression. Tetanus also differs from hydrophobia in the hardness of the abdomen, and in the cause of the wound. In hydrophobia there is commonly more wildness of expression, more movement, more jerking of the limbs, greater apprehension of taking any fluid. The mere approach of a drinking-cup may throw the sufferer into violent spasms.

There is a variety of tetanus, a sort of modification of trismus, described by German writers as *Kopftetanus*, or facial tetanus, the special features of which are that it is caused by some injury to the face, and is attended with paralysis of the injured side of the face. I have seen the following examples of this condition :—(I.) A man, æt. 35, in the Norwich Hospital in 1837 with a wound in the forehead caused by a fall from a cart, lacerating

the occipito-frontalis but not exposing the bone. The symptoms began a week afterwards with stiffness of the neck and jaws, and paralysis of the right side of the face, the mouth being drawn to the left. These were followed by frequent severe spasms of the jaw and body muscles, more especially of the fore part of the body, the man bending forwards and clasping his knees with his hands, this being attended with much suffering and difficulty of breathing. There was no loss of consciousness. He died the day after his admission. The brain presented no morbid appearance. The spinal cord and the mucous membrane of the larynx were rather vascular. (II.) A man, æt. 34, was kicked and wounded about the head and face, December 19, 1858. On the morning of the 27th he could not open his mouth wide. On the following night he was kept awake by sudden closure of the jaws which caused him to bite his tongue. This occurred each night, and was a source of much pain. On the 4th of January he came into Addenbrooke's Hospital. There was a festering wound on the bridge of the nose and scars on the forehead; imperfect power of movement of both sides of the face, especially of the right side amounting to facial paralysis; inability to open the mouth and protrude the tongue; tension of abdominal muscles; voice indistinct; when he tried to speak he put his finger into his mouth to prevent the lips, which were drawn to the left, being pressed between the teeth on the right side; difficulty in swallowing, owing partly to the difficulty in deglutition and partly to the fluid being returned between the lips. The introduction of a tube into the pharynx caused severe general spasm; enemas of beef-tea and port wine were, therefore, given twice daily. The choking and throat spasms caused by accumulation of phlegm in the fauces were much relieved by smoking tobacco. He gradually recovered, and the facial paralysis nearly or quite ceased. (III.) A man, æt. 42, was admitted into Addenbrooke's, March 21, 1891, with a wound under the left eye caused by a kick from a horse. There was paralysis of that side of the face, with clenching of the jaws, abdominal tension, and laryngeal spasms. These last were so severe and almost asphyxiating during the night that tracheotomy was performed, with great relief. On the 23rd he became quiet, but for some days coughing and choking was caused by milk and other fluids passing into the trachea and bronchi, and escaping through the wound in the throat. This gradually ceased, and he got well. During the spasms which occurred under chloroform, and subsequently through the night, the back and limbs, as well as the right side of the face, were affected. (IV.) A strong, healthy man, æt. 28, on February 4, 1895, fell on to a heap of dirt, and cut the cheek just below the left eyelid. The wound was cleaned, dressed, and united by sutures at the hospital. On the 6th it was again dressed and was doing fairly well. On the 10th he felt a little stiffness of the jaws. On the 11th the wound was again dressed, but the stiffness of the face did not attract much attention. On the 12th this symptom had increased. On the 13th he was admitted into the hospital. Milk was given, but he became less and less able to swallow it. On the morning of the 16th, when I first

saw him, the affection had increased considerably. He was unable to open the mouth or protrude the tongue. The attempt to do so caused severe spasms of the face, neck, and back, inducing a certain amount of opisthotonos, also decided spasm of the front of the neck with blueness of the face. There was no hardness of the abdomen and no spasm of the limbs. Decided paralysis of the left side of the face, the mouth was drawn to the right, the eyelids could not be closed, and the left pupil was dilated. He had been able to swallow very little during the night. The case was evidently urgent. Antitoxin was telegraphed for; but before it arrived or other measures were taken he had a severe spasm, during which he became blue and died, evidently from laryngeal stoppage of the breath. On post-mortem examination on the 18th no trace of disease was discovered.

It will be observed that in all these cases, in addition to the wound of the face with paralysis, clenching of the jaws, and tension of the abdominal muscles, there was spasm or paralysis of the glottis which constituted the most urgent symptom. This was fatal in No. IV., probably also in No. I., and required tracheotomy in No. III.; in No. II. the pipe of tobacco seemed to give relief. The paralysis of the glottis permitting fluids to pass from the mouth into the respiratory passages was a very troublesome feature in No. III.; and in No. IV. the pupil was dilated. In I., II., and III. the muscular affection did not extend beyond the abdomen, where it caused firmness of the abdominal wall; but in No. IV. the back muscles were affected, and the abdomen was soft. In all the limbs were free. The facial paralysis is difficult to explain. It has been attributed to swelling or some inflammatory or other influence radiating from the wound and involving the facial nerve, to inflammation of the nerve in its course through the temporal bone or on the cranial side of that bone, but no satisfactory conclusion has been arrived at. In No. IV. the paralysis extended to the iris. There was no loss of consciousness or of sensation in the parts affected in any of the cases.

Rose, in the article before mentioned, gives two similar cases; in one of them the affection extended to the limbs and the patient died; in the other recovery took place. In a case of kopftetanus related by Caretti there was a lacerated, contused wound of the forehead, paralysis of the face on both sides, and trismus. The arrest of the malady was attributed to the use of antitoxin, and another case in which cure was also attributed to antitoxin is quoted. (See also 19.)

Certain cases of *basal meningitis* may sometimes be mistaken for tetanus. In such cases the temperature is a valuable indication. In tetanus the tetanised muscles may be drawn upon without giving rise to pain, but in meningitis any manipulation of the head and neck usually gives rise to great agony. In this latter disease, too, the glands of the neck are often considerably enlarged.

The spasms of *strychnine* poisoning somewhat resemble those of tetanus; but they are more sudden and more rapid in sequence, affecting the whole frame, including the digits. The muscular relaxation in

the intervals of the spasms is more complete. The affection is more quickly fatal, or, on the other hand, subsides; a speedy termination which contrasts with the somewhat slower course of tetanus, especially of those cases of tetanus in which there is no discoverable external lesion. Strychnine may be found in the urine.

Tetany, so-called from its simulating tetanus, is a spasmodic affection resulting from an irritated condition of the nervous centres, either originating there, or transmitted from some disorder of other parts, such as the stomach or bowels, the uterus, the urinary or genital organs. It appears to be less common in this country than in other regions. The spasms progress less steadily and recur less regularly than those of tetanus, and they are attended with less wear of the system. Often they are localised, and not unfrequently they are confined to the hands and feet; this is particularly the case in children, in whom the malady, often associated with rickets, easily yields to treatment, or subsides spontaneously. In some instances the spasms are more general, more severe, or more frequent, and they may lead even to a fatal termination. This has occurred in several cases after complete removal of the thyroid gland, and in these circumstances the diagnosis from tetanus might be difficult. One cause of tetany, at any rate, appears to be a deficiency in the secretion of the thyroid gland; and cases of its cure, either after removal of the gland or otherwise, by administration of the thyroid extract, have been published by Dr. Byrom Bramwell (14). If this sequence be verified, thyroid extract would serve as a ready means of diagnosis. Sudden and fatal attacks of tetany sometimes occur in cases of dilatation of the stomach.

Among the many features which *hysteria* and *hystero-epilepsy* occasionally assume are spasmodic or convulsive seizures; these may present some resemblance to tetanus, but can scarcely be mistaken for it. The sex, appearance, general character of the patient's constitution, and the character of the seizures, are commonly sufficient to indicate the nature of the malady. The writhing, the distortion of features, the laughing or crying, the hallucinations, the more or less complete anæsthesia or paralysis of parts of the body, the affections of consciousness, most of which are due to influences acting on the cerebral hemispheres, are very unlike the manifestations of spinal excitement which we witness in tetanus.

Treatment.—With regard to the treatment of tetanus it is necessary to bear in mind, *first*, that, like most other diseases caused by toxic agencies in the blood, it runs a definite course, having, as it were, a certain life-history—a period of incubation which varies from a few hours, seldom less than twenty-four, to several weeks, a period of increase, and a period of decline. These may not be defined or regular as to their time of occurrence or duration, but they clearly exist; and the severity and impression of the attack upon the system may be taken as proportionate to the amount and virulence of the admitted poison as compared with the resisting powers of the individual. *Secondly*, as already

mentioned, the symptoms of tetanus are usually seen first in the muscles of the neck, jaws, and face, or in the group of muscles near the seat of entrance of the poison. This early condition has been called trismus; and if the affection go no farther the patient commonly recovers. *Thirdly*, we have hitherto, that is to say till recently, known of no antidote or agency whereby the poison could be neutralised or its influence upon the system mitigated. Now, however, we have at command a substance, antitoxin, which possesses the property of neutralising tetanus toxin. *Fourthly*, treatment should be directed to the adoption of measures which may increase the resisting strength of the tissues, and enable the patient to hold on till the malady runs its course and terminates by resolution. The alleviation of particular symptoms, such as the spasms, may do something to diminish the distress, but little to modify the progress of the malady; and the drugs employed for the purpose have, on the whole, often done more harm than good. The only hopeful means of treatment has consisted hitherto in the endeavour to maintain the strength by the administration of nutriment—this being especially indicated by the wasting and exhausting influence which, as already mentioned, forms such a prominent feature of the disease. Unfortunately, in most of the severe cases this cannot be efficiently carried out owing to the difficulty of swallowing; and the difficulty of giving enemas is often such that they cannot be continued, though in some cases they are well borne and should then be persevered with. When food cannot be swallowed recovery rarely takes place, and nothing can be relied on even to postpone the fatal event. A great variety of drugs, chiefly of the sedative kind, have been tried; some have been thought, in particular cases, to have done good, but no decidedly good results have been obtained. Even the relief from distress which may be produced by them does not in the severe cases seem to influence the progress of the malady materially, and the mild cases in which they have seemed beneficial would probably have recovered without them. Electricity, antipyrin, and cold baths have been used, as well as injections of carbolic acid and corrosive sublimate; but the cases in which benefit is reported have been of the mild type. In short, whenever the patient can be induced to swallow, the administration of nutriment should be regarded as the sheet anchor, and no medicinal treatment should be allowed to interfere with it. Unhappily, even in these milder cases it will often fail, and, saving the antitoxin method, we have no hopeful resource. The worst case in which I ever saw recovery was that of an infant from whom I had removed a large fatty or fibro-adipose tumour situated on the back of the neck. The spasms were frequent and so severe that, on several occasions, we thought the child was dead. She continued, however, in the intervals to swallow milk. I did not allow any medicine to be given, but relied exclusively upon the milk. Gradually the spasms became weaker and less frequent, the malady ran its course, and the child recovered. I once went several miles to see a case of tetanus in a man, employed in the stables of a horse-dealer, who had been accidentally

shot in the back of the thigh by his master. I directed the administration of port wine, beef-tea, and eggs, as much as he could take, and prohibited all medicine. It was rather a severe case, but the man got well. I have treated other cases in the same manner and with the like result. All, be it remarked, were able to swallow, though some with difficulty, and were, therefore, of the milder type. It is surprising how much nourishment can be taken and well borne in these cases; this indicates that there is no failure in the digestive and assimilative powers.

Since it has been recognised that tetanus is a specific infective and toxic disease we can put the treatment on a much more definite basis than has hitherto been possible. In the first place, efforts must be made to destroy the manufactory and producers of the poisons, then to neutralise such poison as remains uncombined with the central nervous tissue, and finally to place the patients under such conditions that the irritable nerve centres may be maintained at rest as much as possible. It is now generally recognised that we have fairly definite indications as to the lines of treatment necessary to attain these ends. Moschcowitz, in his summary of treatment, maintains that an attempt should be made:—"(1) To destroy the bacteria at the seat of infection and thereby prevent a further production of toxins; (2) to eliminate from the body the toxins already absorbed from the primary lesion; (3) to neutralise and render innocuous the poison already absorbed; (4) to immunise the body after local infection has taken place; (5) to overcome the symptoms due to the action of the toxins." The first of these objects is achieved by enlarging the wound, free excision, and by the removal of all foreign substances such as fragments of paper-wadding, splinters of wood, and particles of earth. This being done, the wound should be thoroughly disinfected in order to get rid of the tetanus bacillus, and to destroy other organisms which, as Roux and his colleagues have pointed out, play such an important part in assisting the inoculated tetanus bacillus to cause the development of tetanus. The antiseptics recommended for this purpose are acidulated bichloride of mercury, a 1 in 1000 solution, carbolic acid or kresol in 2 to 3 per cent solution, or fairly strong iodine solutions (Lugol's solution) especially those containing 1 or 2 per cent of the terchloride of iodine. According to Babes the use of the terchloride of iodine, which acts as a somewhat powerful irritant, is not always advisable. In certain cases the actual cautery or lunar caustic may be applied with advantage. In such cases great care should be exercised in the after treatment of the wound. In a few cases, especially in those where the tissues are much bruised and where the wound is very dirty and complicated so that proper cleansing cannot be effected, amputation may be advisable and should certainly not be lost sight of as a measure that may be necessary under these conditions. Thus, in a lad æt. 13, admitted into Addenbrooke's a fortnight after a contused wound of the fourth and fifth fingers, the fourth finger, which was in a foul state, was amputated under chloroform, a bad spasm occurring when he was being

anæsthetised. The spasms were not very severe, the temperature never rose above 100° F., and he took nourishment. Chloral hydrate and bromide of potassium were given; the spasms diminished in frequency and severity till April 16, when the last occurred, and he got quite well. Gross relates that in a case of tetanus he dissected out from the face of a girl a tender cicatrix which had followed a lesion from a splinter of wood a month before the occurrence of tetanic symptoms; no further paroxysms occurred. On the other hand I have seen amputation of the leg in four cases in which tetanus ensued upon injuries to the foot, but without good effect in any. A more favourable view of the operation seems to be afforded by the *Surgical History of the War of the Rebellion* in America (*vide* p. 1078), where it is stated that the operation was resorted to in twenty-nine cases after incipient tetanic symptoms had set in, with favourable results in ten. It is not stated whether in these cases the disease was acute or chronic, though it would appear to have been acute in four out of the seven cases related.

If by extraction of one or more teeth, or by the nostril, no way can be made for the passage of a tube, *gastrostomy*, which has been rendered so comparatively safe and simple by modern surgery, might be resorted to in some of those cases of medium severity in which swallowing is difficult or cannot be accomplished. The requisite steps should be taken to open the stomach at once and introduce a tube through which nourishment may be passed with a free hand. I am not aware that this proceeding has been tried or even suggested; but I think it deserves consideration, and it might prove an adjuvant to the *treatment with antitoxin* by maintaining the strength during the days in which that remedy is being employed. A new hope has dawned with regard to the treatment of this affection by antitoxin, and the general opinion seems to be that in many of the cases in which it has been tried it has so far afforded relief as to justify the hope that further experience will show, at any rate, that it has more potency in resisting and overcoming the malady than any other agent which has yet been tried. We read that in cases of the milder kind where it has been tried the spasms have been mitigated, and the amount of toxin in the urine has been reduced. Free diuresis has been suggested as a useful adjunct to other treatment in cases of tetanus. It is thought that some, at any rate, of the tetanic toxin may thus be diverted from the nerve-centres. It has been noted that the symptoms have returned during the temporary suspension of the injections, to be mitigated again on their resumption. A large proportion of the recorded cases in which it has been used have recovered, though, as I have already said, these were chiefly of the milder type (for statistics, see pp. 1060-61); it does not seem to have been productive of ill effects in any of the cases. In most cases the relief afforded by the antitoxin injections, if any, was soon manifested. In some there was a longer interval, the symptoms continuing unabated or even increasing at first, though they ultimately yielded to the influence of the antitoxin. In two cases of "Kopftetanus" referred to above the good results were attributed to the

use of the serum. These and other variations in the effects of the agent may not improbably have depended on variations in its strength and quality or on the method of its preparation. Respecting all this there is much to be learned, and we must look for practical information concerning the antitoxin treatment of tetanus, in the main, to those countries in which the disease is more frequent than happily it is in our temperate regions. It has been suggested that, as the toxin circulates in the blood, an effort should be made to remove some of this toxin by withdrawing the blood from the circulation and injecting saline solution in its place. In this connexion, however, it should be borne in mind that any toxin circulating in the blood-plasma can, in all probability, be neutralised by intravenous injections of antitoxin. It must also be remembered that the leucocytes probably hold a considerable proportion of the toxin that is in the blood-vessels, and that in all probability if venesection should be resorted to under any conditions it would be advisable, in the first instance, to produce a leucocytosis. This, however, seems to be scarcely a practical method of treatment. The alternative of neutralising such tetanus toxin as is contained in the blood by the injection of antitoxin appears to be far more rational. In all these cases it must be borne in mind that before tetanic symptoms make their appearance a good deal of the damage has already been done (*vide* p. 1063). As Marchand, quoted by Moschcowitz, puts it, "the patient with tetanic symptoms is not beginning to have tetanus, he is beginning to die of tetanus." By neutralising the toxin in the circulating blood it is prevented from affecting hitherto unaffected tissues; and as Dönitz has demonstrated, a large amount of circulating antitoxin may attract a certain proportion, at any rate, of the toxin that has already entered into combination with the affected nerve-cells. Roux and Borrel, and Blumenthal and Jacob were of the opinion that if they could only get the antitoxin directly into contact with the nerve-cells and the cerebrospinal fluid it might be possible to neutralise some, at least, of the tetanus toxin contained in such relatively large amounts in these tissues and fluids. But, as already indicated, although the subdural and intracerebral injections are worth trying, and may be carried out with safety, under conditions already mentioned, we must not expect too much from this method of treatment. In carrying it out remember that unless the antitoxin is injected into the lateral ventricles, the amount introduced at any one point should never be greater than 1 c.c.; that the injections should be made exceedingly slowly, and that great care should be taken to disturb (by movement of the needle or of the head) the brain tissue as little as possible. It can scarcely be too strongly insisted, that as soon as tetanus is suspected even, antitoxin in large quantities should be injected at once. There should be no waiting to complete the diagnosis, and when antitoxin is injected the mistake of injecting too small a quantity should never be made. It can do little harm beyond the production of erythema, etc., and it may save the life of the patient. Prophylactic injections are not, as yet, used nearly freely enough. We have an excellent example placed before us

by the veterinarians who have pointed out that in certain animals "castration, amputation of the tail, the ablation of 'proud flesh' or tumours, the operation for cryptorchitis or hernias, and so forth, are often complicated by tetanus. Moreover, tetanus may frequently appear in horses that have received wounds in the foot or in the lower parts of the limbs, 'clous de rue,' farrier's punctures, wireheels, blows, etc.," (Metchnikoff). Most excellent results have been obtained from the use of antitoxin in such cases. Nocard sent out an enormous quantity of antitetanic serum to be employed as a prophylactic, large animals receiving two injections of serum of 20 c.c. each at an interval of ten or twelve days, smaller animals (sheep and pigs) 6 to 10 c.c. The following, according to Metchnikoff, was the result :—"Of the 3088 animals which received the first injection of serum immediately after the operation not a single one developed tetanus. Of the 400 animals which received the first injection at a later period, one to four days and more, after the accidental wound of which they had been the victims, one horse only, treated five days after the accident (farrier's puncture), manifested mild tetanus, and it soon recovered. In the same localities where the results of the injections were so brilliant, 314 cases of grave and fatal tetanus occurred amongst animals operated upon and injured that were not submitted to the serum treatment." This same author, however, utters a very necessary warning note to the effect that, though the efficacy of the antitetanic serum employed as a protective agent can no longer be questioned, it must not be forgotten that its injection does not render the treatment of the wound unnecessary. Wounds should receive a rigorous antiseptic cleansing, and foreign bodies should be carefully extracted, otherwise the prolonged presence of tetanus spores might set up a late tetanus after the disappearance of the transient immunity produced by the serum. In France the prophylactic treatment has now got beyond the veterinarian. "It often happens that bicyclists, in falling, receive injuries which are contaminated by horse dung or other matters which may contain the spores of tetanus. In these cases, as in many other forms of injury, vaccination with antitetanic serum is indicated," and we are informed that people suffering from accidental injuries now present themselves at the Pasteur Institute and ask to be treated with a protective injection of serum; whilst several medical men and surgeons treat with similar injections patients whose wounds have been contaminated by earth or dung. So far as is known, such injections have been attended by nothing but good results. In Prague, Pitha has applied this prophylactic injection for the purpose of arresting an outbreak of tetanus in the Maternity Hospital, where at one time many of the patients operated upon succumbed to tetanus. A systematic injection of the patients who were likely to afford any nidus for the lodgment of the tetanus bacillus soon stamped out the epidemic. Although it is necessary thus to attack the disease at its source, it must ever be borne in mind that the patient should be protected against all irritation or stimulation of the reflex nerve-centres. The unstable or damaged nerve-cells should be excited

as little as possible, the patient should be carefully isolated and protected from light, noises, and jarring and irritation of every kind, whilst the usual medicinal remedies capable of reducing reflex irritability should be given. Amongst these may be mentioned opium, morphine, chloral, bromides, and perhaps also hyoscyamus, paraldehyde, and physostigma. A routine method of treating tetanus patients has been to keep them under the influence of chloroform for considerable periods. In view, however, of the ease and rapidity with which chloroform sets up degeneration with fatty changes in the heart, liver, and kidneys, I should be strongly inclined to deprecate the use of this drug in tetanus, as in these cases the strain on the heart and kidney are necessarily very great and are often prolonged for considerable periods.

When the disease subsides the spasms become less severe and less frequent, the face more natural, and the periods of sleep longer and less disturbed. For a considerable time after all spasms have subsided a sense of stiffness, as if from cold or rheumatism, is experienced in various parts; it is longest felt in the neck, back, and loins, and is liable to be increased by exposure to damp or cold, or by fatigue. It is in some cases felt about the jaws for months. Much care in diet and in the avoidance of cold should be enjoined, for instances have occurred in which the disease has returned after many days, somewhat in the manner of relapsing fever.

Prognosis (see pp. 1060, 1064).—It may be stated generally that the traumatic form of the disease is most fatal, then comes the idiopathic form, and lastly facial tetanus.

Morbid Anatomy.—The examination, post-mortem, in cases of tetanus has commonly revealed to the naked eye few traces of disease in any part of the body. Careful search should always be made for small skin lesions, scars or cicatrices, small abscesses around splinters of wood or iron. The search should extend to the matrices of the nails, the pharynx, and the intestine, though lesions can seldom be made out in these latter positions. Naturally, attention has been directed chiefly to the nervous system; but here, for the most part, whether in the brain, spinal cord, meninges, or nerves, little that is abnormal except, perhaps, some hyperæmia and œdema of the grey matter of the brain and of the cerebral membranes has been discovered. There may also be an accumulation of fluid in the ventricles, whilst small hæmorrhages may be found in the cerebral substance. In a few cases, it is true, congestion has been observed in the anterior horns of the grey matter of the spinal cord, or in its membranes, or in both, more particularly about the regions connected with the nerves of the injured part. This congestion has, in some instances, been attended with changes or degenerated conditions in the grey matter of the cord, and some swelling. Thus an instance is related by Dr. Dickinson (28), in which there was, in addition to the congestion of the dura mater and the pia mater, swelling of the cervical and lumbar portions of the cord caused by transparent exudation into the substance of the cord with consequent lesion of the substance. Lockhart Clarke

and Prof. Clifford Allbutt also found swelling and areas of disintegration of the grey matter of the cord with exudation of finely granular matter and débris of blood and vessels. The nerves in the neighbourhood of the wound have also been found inflamed, and along their course there may be nodular thickenings. "The bronchi are frequently the seat of catarrhal inflammation, the lungs are often œdematous, and in older cases in a state of splenisation inferiorly and posteriorly. The abdominal organs are usually hyperæmic; in older cases we find beginning parenchymatous degeneration of the heart and kidneys. Not rarely there are hæmorrhages in the neighbourhood of the spinal ganglia and in the pericardium" (4). These occasional appearances confirm the view, which on other grounds can scarcely be doubted, that the tetanus poison vents itself in an especial manner upon the spinal cord, causing functional disturbance; though it is usually attended with little or no gross structural lesion. This absence of actual nervous lesion formed an argument (13) against the supposition that the real, at any rate the primary seat of the disease was in the nervous system itself, and prepared us for or suggested the view, since confirmed by bacteriological investigations, that blood-poisoning by noxious material introduced into the system must be the essential cause of the malady.

The *rigor mortis* is said to persist for some time. As already stated, certain muscles have been found ruptured, and even bones broken, by the force of the spasmodic contraction of the muscles.

Infantile Tetanus (*Tetanus neonatorum*)

Is commonly, and probably with reason, attributed to some infection taking place at the umbilicus. I have only seen one case: the child was stiff all over, persistently so, as far as I could judge, and did not live long. Escherich has tried the antitoxin treatment in four of these cases, of which one recovered. In case 1 the doses administered were too small in quantity; in case 4 the disease was exceptionally severe, so that a good result could not be expected; in case 3 the injections had to be discontinued in consequence of the onset of septic pneumonia. Inoculation of mice from two of the cases (1 and 4) with a bit of tissue taken from near the umbilicus caused typical tetanus; but in the other cases the inoculation was without result. The disease is said to be common in some regions, especially in India, where antitoxin has been tried, at least in one case, but with no good result.

APPENDIX

History of the War of the Rebellion.—The fullest statistical record hitherto published is to be found in that marvellous compilation and evidence of American work, the *Medical and Surgical History of the War of the Rebellion*, Part III. vol. ii. Surgical History, p. 818. Of 246,712 injuries by weapons of war 505 (0·20 per cent), or a little over 2 in 1000, were followed by tetanus, which

is regarded as not a large proportion. The seat of the injury and the result are tabulated as follows :—

Seat of Injury.	Total Cases.	Recoveries.	Deaths.	Ratio of Mortality.
Head, face, neck	21	1	20	95·2
Trunk	55	5	50	90·9
Upper extremity	137	18	119	86·8
Lower extremity	292	30	252	89·7
Aggregate	505	54	451	89·3

"The belief that wounds of the foot and hand are particularly liable to cause tetanus is not confirmed by the cases recorded during the war." The rarity of tetanic complications of chest-wounds is noted ; and in all but one of the 17 of these there were injuries to scapula, shoulder, or arm.

In 131 instances tetanus followed closely upon operations on the extremities, namely, in 116 cases after amputations, and in 15 after excision.

The recoveries were chiefly in the slighter or more chronic cases ; and the later the occurrence of the disease after the injury the greater the chance of life. In 6 cases the disease occurred within twenty-four hours after the injury. Few on the second, third, and fourth days. From the fifth day the number rapidly increased until the eighth, when it diminished till the fourteenth day ; after which it "appeared irregularly"—in one not till seven months after the injury. The duration of the disease is given in 358 cases ; in 203, or more than half, it did not exceed three days, and of these only two recovered. The longest duration among the fatal cases was twenty-seven days.

In several instances the removal of the missiles, foreign bodies, or pieces of bone seemed to have quieted the threatening symptoms.

Amputation was resorted to in 29 instances after incipient tetanic symptoms : 10 of the cases resulted favourably. This is very strong evidence in favour of the proceeding ; but it is not stated whether the disease was acute or chronic. In 4 of the 7 cases related it would appear to have been acute. Relief was afforded by the chloroform and continued after the operation. No anatomical lesions of the medulla oblongata, cerebellum, or spinal cord were found in the cases that were examined post-mortem.

George Murray Humphry, 1896.
G. Sims Woodhead, 1905.

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ENTERIC FEVER

By Professor JULIUS DRESCHFELD, M.D., F.R.C.P.

The Sections on Bacteriology and Paratyphoid Fever

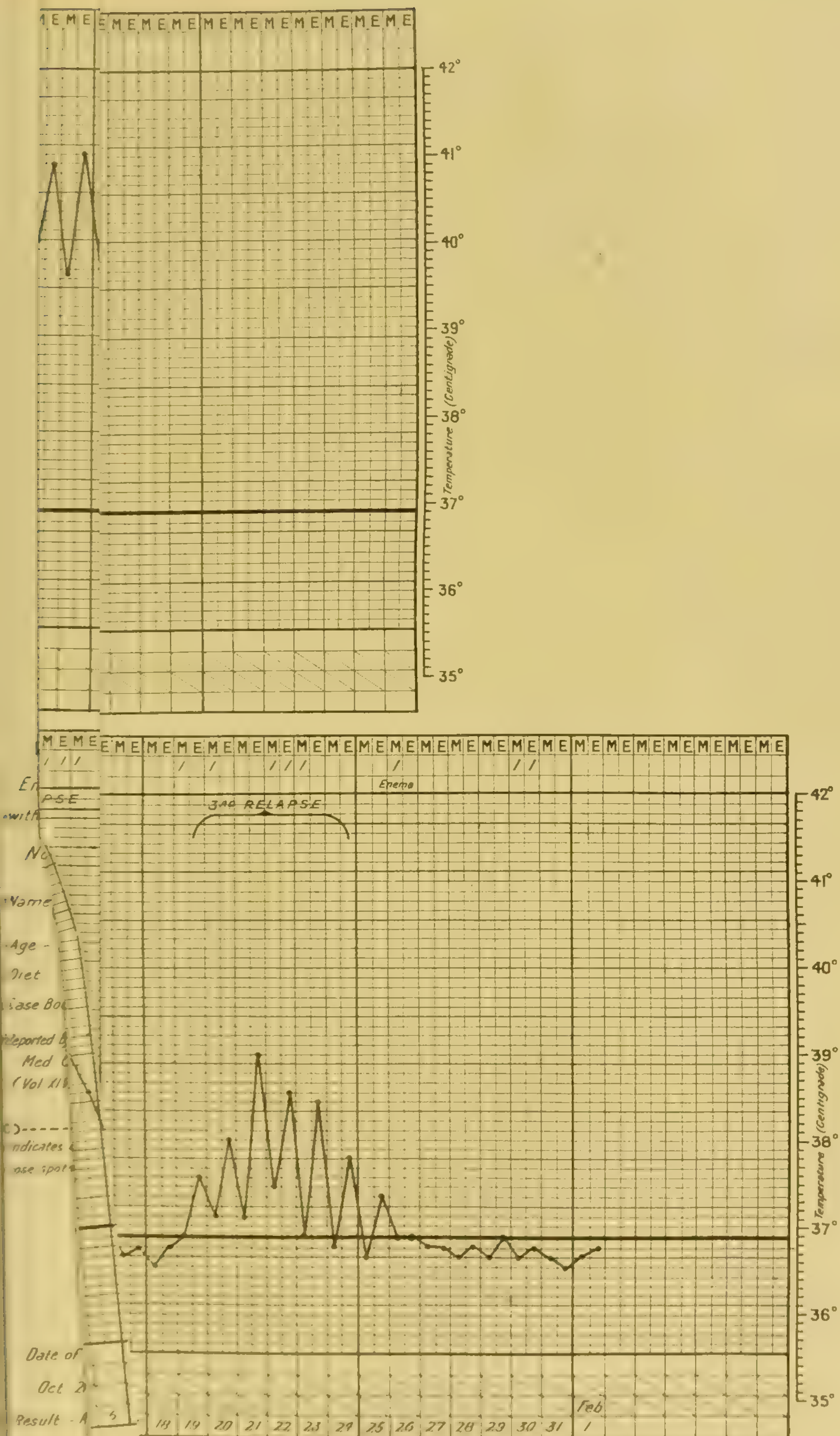
By Professor J. LORRAIN SMITH, M.D.

SYNONYMS.—Gastric Fever, Typhoid Fever, Pythogenic Fever; Fr. *Dothiénentérite, Fièvre typhoide;* Germ. *Abdominaltyphus, Nervenfiebre.*

Definition.—An acute infectious fever, due to a specific micro-organism, occurring endemically, sometimes epidemically; *clinically* characterised in ordinary cases by a gradual onset, followed by a period of continuous fever with diarrhœa, an enlarged spleen, tympanites, and a roseolar rash, usually lasting three weeks; *anatomically* characterised by more or less extensive hyperplastic inflammation and ulceration affecting the lymphoid elements of the intestines, with swelling of the mesenteric glands and enlargement of the spleen.

History.—Enteric fever appears to have been known to the ancient writers (for example, Hippocrates and Galen); but it was not until the beginning of the nineteenth century that it was distinguished from other acute febrile affections, especially from typhus.

In Germany Von Hildenbrand (1810) clearly distinguished these two affections; in France Bretonneau (1813) proposed the name of dothiénentérite, to denote the specific nature of its intestinal lesion; Louis (1829) gave the name "typhoid" to the fever; in America Gerhard and Pennock (1837) first clearly differentiated between typhoid and typhus fevers; whilst in England, after some older writers, the observations of Perry (1836), Barlow (1840), Stewart (1840), and especially the classical



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papers published by Sir Wm. Jenner (1849-53), led to the final distinction between the two diseases, which ever since has been universally recognised. Enteric fever having then been recognised as a specific fever, its etiology was made the subject of further investigation. Its infectious nature, and its propagation by the fæcal discharges of the patient, led many physicians, headed by Budd, to look upon it as due to one specific agent, and to deny its origin *de novo*.

The advances made in sanitary science, the establishment of special sanitary medical officers, and the interest with which all matters relating to public health were considered by corporate bodies, a movement in which England took a prominent part, led on to investigations into the cause or causes of enteric fever; and though the agent was not discovered, yet the source of the propagation and dissemination of outbreaks were carefully studied, and many of them were traced to contaminated water or milk and to "sewer gas." This led to the improvements in drainage and water-supply of many English towns, with the result of a marked diminution in the prevalence of enteric fever, and of an almost total extinction of typhus (see Table I. Appendix). With the development of bacteriology the history of typhoid fever entered upon a new stage.

Murchison, whose classical writings on the continued fevers of England still maintain a prominent place in the literature of enteric fever, believed in the origin of enteric fever from decomposing organic material, and also in its spontaneous origin. The observations of Stich and later of Panum, which showed that the ingestion of putrid material may produce, amongst other symptoms, fever, diarrhœa, and intestinal lesions, not only supported this opinion, but gave rise to that of the autogenetic origin of enteric fever, namely, that the disease may be generated in the system from decomposition of fæces in the intestinal canal without any infection from outside.

Eberth (1880) discovered a peculiar bacillus in the organs of persons who had died of enteric fever, and subsequent investigations not only confirmed this observation, but placed the pathogenetic nature of this organism, and with it the etiology of enteric fever, on a firm basis; thus the pythogenetic hypothesis of Murchison and the autogenetic hypothesis of other observers became untenable.

In sketching the history of enteric fever the progress in the treatment of the disease must not be forgotten. Whilst depletion and starvation were for a long time the guiding principles in the treatment of fever, the liberal use of stimulants was advocated chiefly by British physicians (Alison, Graves, Todd, and Stokes); but in the course of time their administration was again restricted, and used only on definite indications. The antipyretic treatment by the cold bath, however, first recommended by Currie (1787) and resuscitated by Brand (1861), has diminished considerably the mortality from enteric fever, and is now widely adopted. The various antipyretic drugs have been extensively employed, but have not displaced the cold water treatment. With the

discovery of the typhoid bacillus new methods of treatment have been tried: the antiseptic treatment proposed by Bouchard (though antiseptic drugs had been given long before in enteric fever), and subsequently adopted in various forms by many English and continental observers; and more recently attempts have been made, and with some promise of success, to find a specific treatment, both curative and prophylactic.

Geographical Distribution.—Enteric fever prevails all over the globe. It is endemic in Great Britain, but is less common in Scotland than in England or Ireland; its frequency in the British Islands has, however, considerably diminished during the last twenty to twenty-five years, owing to better sanitary arrangements. It is met with throughout the whole of Europe; it is widely distributed throughout the whole of the United States and Canada; it is met with in India, Africa, and in Central and South America. J. D.

Bacteriology of Enteric Fever

Historical Sketch.—The problem of the unity of enteric fever assumes new forms as investigation advances, and the multitude of researches which have been carried out on the subject are best understood when we consider them as steps towards the final solution.

Before the disease was investigated from a bacteriological standpoint, it had been found impossible by a study of the morbid anatomy and clinical symptoms of the cases to decide whether enteric fever is a single specific pathological condition or a group of closely similar diseases. Nor has the subsequent work of clinicians and morbid anatomists cleared up the difficulty. It is in view of this unsolved problem that we have to consider the contribution to the pathology of the disease which the direct study of the etiology, by bacteriological methods, has afforded. I propose therefore to give, in the first place, a short sketch of the development of the etiological investigation, and then a detailed account of our present knowledge of the bacillus typhosus and of the bacillus paratyphosus.

Eberth in 1880 described the bacillus typhosus as it occurs in the mesenteric glands and spleen of persons dying of typhoid fever. He did not succeed in isolating it, and therefore did not obtain a full description of its cultural characters. The investigation was carried on by Gaffky, who in 1884 was able to publish a detailed account of the bacillus. The appearance of a culture on potato he regarded as a most essential means of differentiating it from allied forms of bacteria occurring in the intestine. At the same time he described a series of experiments directed towards the discovery of the pathogenetic power of the bacillus. Gaffky's experimental investigations, however, consisting of feeding animals (including monkeys) with food infected by the bacillus, and of injection of cultivations into the blood-stream, gave only indecisive results. About the same time (1885) Fraenkel and Simmonds obtained more positive results in their experiments with guinea-pigs, mice, and

rabbits, by using larger quantities of culture and by cultivating the bacillus on potato; Gaffky having used serum as the nutrient medium. The effects observed by Fraenkel and Simmonds were paresis, loss of appetite, and diarrhœa. Death occurred at a period varying from two hours to four days after the injection. The changes in the viscera of these animals observed post-mortem were swelling of the spleen, mesenteric glands, Peyer's patches, and sometimes of the solitary follicles of the intestine, and cloudy swelling of the liver and kidney. The bacilli were found distributed in the tissues. The changes were most distinctly seen in animals which had received intravenous injections. From these results they concluded that they had obtained experimental proof of the pathogenicity of the typhoid bacillus. While, however, the bacillus was pathogenetic, the similarity of the symptoms of the infected animal with those of human typhoid was not sufficiently close to justify these authors in describing the condition produced in the animals as typhoid fever. The bacillus and its products when cultivated may be toxic or pathogenetic, but they are not nosogenetic in animals. Subsequent investigators have taken up this problem, and have analysed these observations by further experiments bearing on the effect of toxins in producing the result, on the variations in virulence amongst races of typhoid bacilli, on the means by which virulence can be raised, etc. As regards ordinary domestic animals used for experiment nothing further has been reached, except a more consistent explanation of the effects which Fraenkel and Simmonds originally obtained. The failure to reproduce typhoid fever, as such, in animals has been, and remains, a constant source of difficulty in the investigation of the disease. Professor Grünbaum (144) has recently published a preliminary account of a series of experiments on the chimpanzee. The completion of this research will be of great interest.

The discussion of the typhoid bacillus reached a farther stage with the discovery of the bacillus coli communis by Escherich in 1885. The general similarity of this bacillus to the bacillus typhosus, both in its morphology and in the fact that it is distinctively an intestinal microbe, led to important investigations. It became necessary to work out a series of clearly defined tests by which the bacillus coli communis could be distinguished from the bacillus typhosus. Further, since the bacillus coli is present in the intestine in all cases of typhoid fever, it became necessary to determine its relation to various pathological conditions which more or less clearly simulate typhoid fever. For a time some investigators believed that there was a very close relationship between the two kinds of bacilli, and that it was possible, even if they were distinguishable, that one form could be transformed into the other. The intimate association of the two microbes in the intestine also led to a method of using the commoner and hardier bacillus coli as a guide to the situations and conditions in which the elusive bacillus typhosus might be found in the external world. Generally speaking, the bacillus coli communis has more vigorous powers of growth than the typhoid bacillus.

disintegrates proteids and carbohydrates more actively, and shows generally a wider power of fermentation. On this broad principle there has been founded a series of distinguishing tests by which the two forms are clearly differentiated. In comparing the two kinds of bacilli, however, it should be noted that morphologically the races of typhoid bacilli from various sources are more or less completely indistinguishable from each other. We may indeed yet discover the means of proving that there are morphological varieties of the typhoid bacilli; but so far it is only in their physiological reactions that clearly defined distinctions have been established. On the other hand, the races of bacillus coli communis vary so much morphologically that it has never been settled what exactly the group includes. Hence we speak of intermediate forms. These intermediate forms, which are pathogenetic to man, and have chiefly the characters of the B. typhosus with a few of those of B. coli added, are called *paratyphoid* bacilli. Others which show a closer similarity to the typical coli bacilli are included in the group as coliform, etc. We are chiefly interested in the pathological grouping of these various forms in relation to corresponding types of disease. This grouping began with the discovery, in 1888, by Gaertner, of a bacillus which gives rise to grave symptoms of meat poisoning, and is associated with meat obtained from cattle dying of a form of intestinal inflammation. While these symptoms were widely different from those of typhoid fever, the bacillus enteritidis, as Gaertner named it, was in few points morphologically dissimilar. It had a feeble power of fermenting carbohydrates and proteids, but came far short in this of the typical B. coli. It was subsequently isolated in a large number of epidemics of meat poisoning, and finally, in January 1905, Dr. Klein (145) showed that a bacillus morphologically indistinguishable from Gaertner's bacillus is fairly common in milk. In 39 samples of milk examined, he found it in 25 per cent. It exists therefore in an apparently harmless form over a wide distribution. The study of this bacillus and its various relationships (agglutination, etc.) with the typhoid bacillus, by Nocard, Durham (154), and others, has greatly increased our knowledge of the subject of typhoid infection.

After Gaertner's discovery the next important extension of our knowledge of the bacteriology of enteric fever was due to the work of Sanarelli (146), published in 1892-94, and to a simultaneous investigation by Chantemesse and Widal (147). Sanarelli was struck by the fact that the bacilli isolated from the spleen of patients are in many cases so attenuated that they have little or no effect when injected into animals. He accordingly endeavoured to discover the means by which the typhoid bacillus may be enabled to acquire virulence. This he sought in the action of accompanying bacilli, and in particular of the B. coli. The grounds for regarding this as a natural experiment are two-fold. The bacillus coli increases in number enormously in the small intestine in cases of typhoid fever, and at the same time it acquires an unusual degree of virulence. It might therefore be fairly regarded as an adjuvant of the

typhoid bacillus, and to show how this action might take place, Sanarelli injected the sterilised toxic products of B. coli from an old culture into the peritoneal cavity of a guinea-pig, and at the same time inoculated the animal subcutaneously with 5 c.c. of a typhoid culture 24 hours old. The animal died in 12-14 hours, and typhoid bacilli were isolated from its peritoneal cavity. These bacilli were shown to have now acquired an increased degree of virulence, and when they were subsequently injected into another guinea-pig with an accompanying dose of coli products less than the 10-12 c.c. required for the first experiment proved fatal. After repeating this experiment sufficiently often, he was able to obtain the fatal result with the typhoid bacilli alone. Sanarelli does not regard this adjuvant action as confined to the bacillus coli. Various kinds of bacteria, or even mixtures of them, provided they formed indol in the culture fluid, have this power. Chantemesse and Widal obtained similar results with the sterilised culture fluid of streptococcus pyogenes.

We are probably as yet unable to appreciate fully the value of these results either from a practical or from a scientific standpoint. Whatever their value may be, however, the fact remains that this action does not take place in animals in natural conditions.

The next advance in the study of typhoid fever was due to the application of the principles of Pfeiffer's immunity reaction *in vivo* to the study of the serum of typhoid patients, and typhoid-immune animals. Gruber and Durham (148) discovered that the serum of typhoid patients causes agglutination in a recent culture of the bacillus. Not a little of the importance of this discovery lies in the fact that since the serum reaction is one of the essential phenomena of typhoid fever, and since the same reaction is obtained in animals by inoculation, we have in this experiment a substitute for the complete reproduction of the disease in animals by inoculation. The details of the researches dealing with this subject will be fully described in Prof. Ritchie's article on "Immunity" in vol. ii., and the technique of its application for diagnosis is given in Dr. Drysdale's article on the "Examination of the Blood," p. 692. We are here concerned with the contribution which this method of investigation has made to the etiology of typhoid fever. An account of the work of Gruber and Durham appeared in 1896, and much investigation was carried out; in the first instance, in order to perfect the method for practical application, and, in the next place, to enable it to be used as a clue to the pathology of typhoid infection. Gruber admitted from the first that the serum of man and animals agglutinates various microbes if applied in normal concentration, and that it was necessary to find the degree of dilution at which agglutination ceased, in order to discover the presence of specific agglutinins in a given case. Widal, whose name has been given to the reaction, was firmly convinced of its specific character, and as late as 1903 speaks of it as rigorously specific. With further investigations doubt, however, gradually arose as to the specific character of the reaction, and evidence was brought forward to suggest that it might be produced by micro-organisms other than the bacillus typhosus.

As regards B. coli, Stern (149) in 1898 showed that at low dilutions the serum of typhoid patients causes agglutination. In 1899, Dr. Tennant and I (150), working on the cases in a typhoid epidemic in Belfast, showed that not only does the serum of a certain proportion of typhoid patients agglutinate B. coli, but various races of B. coli agglutinate in the same serum in various degrees. Some races of B. coli showed practically no reaction to the typhoid patients' serum. Others with a tendency to spontaneous agglutination could not be used. However, we were able to obtain intermediate forms which do not spontaneously agglutinate, and which, nevertheless, give a reaction in a certain percentage of typhoid cases.

Dr. Durham (152) had also shown, in the research already described, that the serum of typhoid patients agglutinates the various races of the Gaertner group of bacilli. To this relationship of the serum to the two kinds of bacilli he gave the name of "mutual reaction."

In 1896 Achard and Bensaude (154) described a bacillus which they had isolated from each of two cases. In the first case, the patient, a woman of twenty-four, suffered from a typhoid-like ailment, and while the examination of the blood and fæces gave no unusual result, they obtained from the urine a culture of a bacillus which agglutinated with the serum of the patient, and which, from its close similarity to the bacillus of Eberth, they called the paratyphoid bacillus. The second case was that of a child in whom, after an attack of a typhoid-like fever, suppuration appeared in the sterno-clavicular joint, and from this source the same bacillus was obtained. In 1897 Gwyn, and in 1900 Cushing, both in America, isolated from cases a bacillus belonging to this group. In 1901 Schottmüller described five cases of typhoid-like fever due to bacillus paratyphosus, and in 1902 Conradi, Drigalski, and Jürgens (157) described an epidemic outbreak of 38 cases in Saarbrück. The discussion of this subject brings us to the immediate problem of present-day research.

The Typhoid Bacillus.—The isolation of the typhoid bacillus from the spleen of patients who have died from typhoid fever is a matter of comparative ease. The following simple method is usually successful. The spleen is placed on the table, and with a hot iron the surface is seared to destroy any bacteria lodged there. A knife and pair of dissecting forceps are prepared by steeping in carbolic lotion, and immediately before use they are dipped in a beaker of boiling water to remove the lotion. A piece of tissue is then excised from the centre of the seared area, and this is rubbed on the lower glass of sterile Petri's boxes, in a series, the quantity of material left increasing or decreasing from box to box. Melted agar (40° C.) is immediately poured over this material, the two are carefully mixed, and then allowed to set. The plates are incubated at 37° C., and in 12-24 hours characteristic colonies are usually obtained.

The bacillus can be isolated with equal ease from the gall-bladder. The surface is seared, and a sterile pipette is inserted through the seared area, and agar plates are made with a varying quantity of bile. The

bacilli can also be obtained, though not so easily, from the mesenteric glands and Peyer's patches.

Of great practical importance, for the purpose of diagnosis, is the isolation of the bacillus from patients during life :—(1) The most important method at present in use is the examination of the blood. A syringeful of blood (5-10 c.c.) should be withdrawn from a vein, and planted forthwith on agar. It is now asserted that this method enables the diagnosis to be made earlier than any other, and that its failure in former days was due to the fact that too small a quantity of blood was taken. Castellani in 14 cases had 12 positive results, or 85 per cent; Schottmüller in 220 cases, 82 per cent; Auerbach in 10 cases, 70 per cent; Stern in 38 cases, 65 per cent; Krause 80 per cent. It is clear, therefore, that this method of diagnosing typhoid fever, since it gives an average of 75 per cent of positive results, must be regarded as one of the most certain. Unfortunately, it cannot be used with sufficient ease to make its application universal.

(2) The typhoid bacillus can also be isolated by puncture of the spleen. This method, from which good results as regards diagnosis have been obtained, has been considered as unjustifiable since Haedke's (158) case of subsequent bleeding occurred. Adler (159) records 300 cases without any bad effects, and with the unequalled record of 95 per cent of positive results, and in 90 per cent of these the observation led to an early diagnosis. In spite, however, of Adler's recommendation the general adoption of this method is improbable.

(3) Another available method is that of cultivation of the bacilli from the rose-spots in the skin. Krause records 16 cases, in 14 of which, or 87 per cent, he obtained the typhoid bacillus. Neufeld in a series of 14 cases obtained positive results in 13. The method by which this is carried out is to sterilise the skin at the area of the spot, and obtain a drop of blood or lymph by means of a small incision, or in case of any difficulty in obtaining the blood, to place a drop of sterile bouillon over a spot, and then make a puncture or scratch. Even if there is no free flow of blood there is sufficient admixture of lymph with the bouillon to make the inoculation of the bouillon fairly certain. There is naturally some risk of contamination, from the skin, with micrococci, the complete removal of which is frequently difficult.

(4) The isolation of typhoid bacilli from the fæces of patients has from the first occupied the attention of bacteriologists, and numerous attempts have been made to devise a method by which to secure the bacillus with comparative certainty from among the multitudes which flourish in the intestine. Attention has been called to this problem more particularly lately by the success of the work of the Trier Typhoid Commission (160) with the method of Conradi and Drigalski. Before, however, describing this method, earlier attempts to solve the problem should be shortly referred to. Pfeiffer (161) was the first to obtain cultures of the typhoid bacillus from the intestine by the use of agar plates. Soon afterwards Fraenkel and Simmonds (162) also succeeded, by the use of

gelatin plates. Holz added to the gelatin the juice of potatoes. Elsner added to the Holz medium 1 per cent iodide of potassium. Piorkowski mixed with gelatin 3·5 per cent alkaline urine and 0·5 per cent peptone. Carbolic acid (up to ·05 per cent) has been used also to restrain the growth of other micro-organisms. In recent years, however, attention has been mainly paid to the method of Conradi and Drigalski (163), which was devised to bring out two points: (1) the power of the typhoid bacillus and the bacillus coli communis to grow in a medium to which a small percentage of crystal violet has been added, while the growth of other bacteria is more or less inhibited; and (2) the power of fermenting lactose which is possessed by B. coli but not by B. typhosus. This point is brought out by the addition of litmus as well as lactose to the medium. The basis of the medium is 3 per cent agar, to which peptone and nutrose have been added. Careful directions are given as to the mode of preparation. The medium should, when poured out in Petri's boxes, have the clear blue colour of alkaline litmus. The material to be tested for the presence of B. typhosus or B. coli is planted on the surface of the medium in the plate, and in twelve hours the B. typhosus grows in moist transparent alkaline colonies, and the colonies of B. coli in more opaque and more vigorous acid colonies. This method has been extensively tested, and it has been found to yield about 60 per cent of positive results in the examination of typhoid fæces for the presence of the typhoid bacillus.

Jürgens (164) gives a most instructive account of the post-mortem examination of two cases at Trier. In the first case, the fæces of the patient had been examined without positive result for six days before death, which took place in the second week of the disease. Half an hour after death the intestine was carefully searched. In the duodenum there were innumerable typhoid bacilli, and the bile also swarmed with bacilli. In the lower part of the ileum, where there was marked swelling of the lymphoid tissue, there was a distinct decrease in the number of typhoid bacilli. In the colon they were again greatly increased, but they were nowhere so numerous as in the duodenum, and it is conceivable that in any given mass of fæces they might be absent. A similar result was obtained in a case fatal at the beginning of the fifth week. We may therefore learn from further investigation why the examination of the fæces yields positive results in only 60 per cent of the cases. From the practical point of view a note of the time necessary for an examination is of interest. Twelve hours may be allowed for the development of the characteristics of the bacillus and its colonies on the plates. Likely colonies should then be planted in glucose agar, and cultivated for twelve hours in order to ascertain whether there is absence of fermentation, and at the same time a broth cultivation of the colonies should be tested by typhoid-immune serum of great potency, for the reaction of agglutination at a high dilution. These observations afford the main elements in a rapid definition of the bacillus, and they can be fully made out in about twenty-four hours.

Krause (165) suggests that the explanation of the absence of the

bacilli in $\frac{1}{3}$ of the cases may be due to the fact that where there are few ulcers few bacilli will be found in the intestinal contents, and advocates the use of a method which will relatively increase their numbers. The method of Lentz and Tietz (166) may be used for this purpose.

In about 25 per cent of the cases, according to Neufeld's (167) results, the bacillus may be isolated from the urine. They usually appear there about the end of the second week of the disease.

Typhoid bacilli have been isolated from the bronchial secretion, and also from areas of pneumonic consolidation, in cases of typhoid fever. They have also been found as the cause of suppuration in abscesses in various parts of the body. Such formations occur most frequently in bones, chiefly in the periosteum, but also in the medulla and in joint cavities. With this type of lesion we may group the meningitis which occurs in certain cases.

Characters of the Bacillus.—The bacilli, and especially those from recent cultures, when examined in the hanging drop, are seen to possess a marked degree of motility. The bacillus is provided with a large number of wavy flagella attached to its sides and ends. These are easily stained by any of the methods described in the text-books of bacteriology. It is to be observed that the flagella are, as a rule, more numerous (8 to 12) than those of B. coli (4 to 6). They are also longer, more wavy and delicate, and more easily stained. The bacillus measures 2-4 μ inches in length, and ·5 μ in thickness. In the body larger forms are observed, and the same tendency to form filaments is seen as in cultures. These filamentous forms have not the rapid motility of the shorter forms. In motility the typhoid bacillus differs from B. coli, which, as a rule, has very little if any. This lack of motility, however, is not observed in all varieties of B. coli. The bacillus typhosus from a recent culture stains in a uniform manner, and with the ordinary anilin dyes. It does not retain the stain by Gram's method, nor is it acid-fast. There is, accordingly, no specific method of staining it. In old cultures a moniliform appearance may be observed. This, however, is due to involution and not to spore-formation.

The appearance of the growth in various media has been carefully studied. In broth, the culture produces in a few hours a uniform turbidity without pellicle or sediment. On agar plates the colony has a comparatively delicate transparent appearance with crenated edges. The same general character is seen in a cultivation on sloped agar. The growth is thin, spreading, and, as a rule, in a moderately transparent layer, but sometimes it assumes a mother-of-pearl, or even a whitish opaque appearance. When planted in a stab-culture growth takes place all along the track of the needle. Partial, or even complete absence of oxygen does not inhibit the growth of the bacillus. It is a facultative anaërobe. It grows very feebly on agar in oxygen at a pressure of three atmospheres. The characters of the growth on gelatin are generally similar to those on agar. A fine spreading layer of growth with crenated edges is observed both in the colonies on the gelatin

plate, and in the sloped gelatin tube. The gelatin is not liquefied. On potato the growth varies in appearance with the reaction. If it be acid, the growth is invisible. If it be alkaline, the growth is faintly brown. Very great importance was attached to the growth on potato in the earlier descriptions of the life-history of the bacillus. Other details observed regarding the growth of the bacillus are chiefly negative. It does not coagulate milk nor form gas-bubbles from any of the sugars, nor does it form indol from peptone in broth.

Yet Petruschky (168) showed that a certain slow fermentation of lactose does take place in litmus-whey. Péré (169), on the other hand, failed to confirm this result, but found that the typhoid bacillus can ferment galactose, arabinose, lævulose, and dextrose, producing a lævo-rotatory acid, while B. coli from adults produced a dextro-rotatory acid. This distinction requires further confirmation. The power which the typhoid bacillus possesses of fermenting sugars is manifested only in media specially prepared to bring out this activity. It may be obscured by the simultaneous production of alkali from peptone. Similarly also the production of indol does not take place in bouillon in ordinary circumstances; but Peckham has shown that if the bacillus be planted in peptone solution free from carbohydrate, and transferred to a new tube of this solution every three days, it will acquire the power of producing indol. The bacillus coli which has marked power of producing indol fails to do so if lactose be present in the medium, and generally it is found that bacteria consume as food the carbohydrate present in the medium before they attack the proteid. The typhoid bacillus is therefore no exception to this rule.

Professor Sidney Martin (170), in investigating the nature of its toxin, found that the typhoid bacillus had a feeble digestive action. In agar tubes to which neutral red has been added the bacillus typhosus grows without changing the colour. Typical B. coli cultures cause a green fluorescence in 24 to 48 hours. In this respect, however, B. typhosus resembles many allied forms other than B. coli. A degree of uncertainty consequently still attaches to these tests for the differentiation of the typhoid bacillus from the increasing group of its allies, and much work remains to be done in order to clear up the whole question of the digestive and other changes in media which are associated with bacterial growth and used as differential tests. In recent years the differentiation of B. typhosus from allied forms has been carried out much more by biological tests than by cultural reactions.

Experimental Investigation of Typhoid Fever.—The attempt to reproduce typhoid fever in animals has, as already pointed out, been a comparative failure. Extensive researches, however, have been carried out with a view of defining the nature of the toxic action which the bacillus exerts when it is injected into animals, or when it is given by the mouth. In man, a small dose of bacilli taken by the mouth brings about a specific process due to settlement of the bacillus in the intestine and the lymphoid tissues in its wall. The bacilli multiply there and

then escape into the blood, and become distributed generally in the body. The intestine of man seems to have little of the protective power possessed by that of animals. On the other hand, the blood and lymph of man and of animals react, as we have seen, in a comparatively similar manner. Hence great interest attaches to subcutaneous and intraperitoneal injections in animals. The effects of such experiments have been carefully studied, and Seitz showed that the effects described by Fraenkel and Simmonds, in the research already mentioned, could be obtained by injections of sterilised cultures into the peritoneum. In the next place, Beumer and Peiper (171) showed that several kinds of saprophytic organisms caused the same effects as the typhoid bacillus when injected intraperitoneally.

Sirotinin (172), in a further investigation on this subject, again showed that the effects were due to intoxication, and that cultures sterilised at 100° C. had the same effect as living cultures. In the cases where he injected living cultures into the veins, the bacillus disappeared from the blood the more completely the longer the animal lived. The bacilli survived in the bone-marrow longer than elsewhere, but remained for some time also in the liver and spleen. Further, he confirmed the observations of Beumer and Peiper that bacilli other than the bacillus typhosus give similar results.

An important investigation by Pfeiffer and Kolle (174) on intraperitoneal inoculation showed that the results of inoculation depended on the amount of the dose and the virulence of the culture. They found that fresh cultures from recently isolated races of bacilli are the most actively toxic, while bacilli kept in the laboratory for some time lose their power. Administration of a relatively large dose produced a rich, serous, sometimes blood-stained exudation from the peritoneum, in which the bacilli multiplied. After a rise in the first hour the temperature fell, and death took place in from six to eight hours. The bacilli were found in small quantities in the blood and organs, but in large quantities in the peritoneal exudate. If a small or minimal dose were given, there was a purulent exudation, and not much increase in the number of bacilli, many of the bacilli being incorporated in the leucocytes and undergoing disintegration there. The animal died in two or three days. The blood and organs were in these cases free from bacilli, and the process of destruction was rapidly proceeding in the peritoneal exudate. If the dose were still smaller, the animal was saved by this protective mechanism. At the same time Pfeiffer and Kolle showed clearly that the toxic substance is intracellular, or contained in the bodies of the microbes. The germ-free culture fluid had little or no toxic action, while a small quantity of sterilised culture on agar, of quite recent growth, was toxic. The observations on the human subject correspond with these experimental results. The bacillus is discovered most commonly in the lymphoid tissue of the intestine, mesenteric glands, spleen, liver, and bone-marrow. In the liver, it is seen in small masses occupying a lymph-channel, and surrounded by a zone of necrosis. The multiplication of

the bacillus in the blood with the formation of bacterial emboli has not been observed. The same localisation is seen in the skin in roseolar areas, where there are small areas of necrosis round groups of bacilli occupying the lymphatics of the skin papillæ (E. Fraenkel) (175). These foci are analogous to the necrotic areas in the liver and kidneys. Typhoid fever may, as Neufeld suggests, be placed midway between septicæmia, where the staphylococcus or other causal microbes are very little affected by the blood, and cholera where the micro-organism is so completely destroyed that it is not found in the blood, or deposited in any of the viscera.

The human and animal organisms differ neither in the bactericidal influence of the blood on the bacilli, nor in the effects of the toxin set free from the bacilli, but in the fact that the human intestine is relatively devoid of power to destroy the typhoid bacillus.

Investigations on the nature of the *bacterial toxins* have not as yet yielded many important results. Brieger, in the first instance, isolated from cultures two months old a base which he named typho-toxin. Later, in a paper published with Fraenkel, the separation of a tox-albumin was described. Sanarelli regarded the toxic action as due to a group of substances which he obtained by cultivating a virulent bacillus in glycerin-bouillon for a month, and then macerating the bacilli at 60° C. When this mixture was injected subcutaneously in a dose of 1·5 c.c. per 100 grammes of body-weight, it caused death in a guinea-pig in twenty-four hours. The post-mortem changes were enlargement of the spleen, peritoneal exudation rich in leucocytes, congestion of the intestine, and especially of the lymphatic nodules in the mucous membrane. Prof. Sidney Martin also found that the intracellular toxins obtained by maceration of the bodies of the bacilli are more active than those obtained from the filtered broth. The effects of injection, however, were not different from those due to the injection of products similarly obtained from virulent forms of B. coli, B. enteritidis, or even of vegetable toxins such as ricin. Drs. A. Macfadyen and Rowland (176) have recently published a preliminary account of an investigation on the toxins of the typhoid bacillus. These toxins, as all investigators on the subject have pointed out, are intracellular, and can only be obtained when the bodies of the bacilli are dissolved or broken up. Drs. Macfadyen and Rowland adopted the method of mechanically breaking up the bacilli after they had been frozen by the cold of liquid air (– 180° C.). The disintegrated mass was freed from insoluble suspended particles by centrifugalisation, and an opalescent fluid, composed of the juice of the bacterial cells, was obtained. The fluid when injected into an animal was toxic even in small quantities. The immunising power of this fluid was then tested, and it was found that the blood of monkeys which had been injected with it had both antitoxic and antibacterial properties. The serum protected animals against the effects of injections both of bacilli and of the intracellular toxins. It is generally recognised that the pathogenetic effects of typhoid infection are due essentially to the disintegration and solution of the

bacilli by the blood and other fluids, and the setting free thereby of the toxins contained in them. It was found, however, by Pfeiffer that when small doses of bacilli were injected into an animal, the immunising power of its serum which resulted was against the microbes only, and not against the toxin. A solution of the toxin can be obtained if the bodies of the bacilli are disintegrated by heating to 60° C. for a few minutes. Toxins obtained by this method, when injected, induced in the serum an immunity anti-microbic but not antitoxic. Similarly, the toxins naturally set free from the bacilli invading the blood in a case of typhoid fever create in the patient's serum the bodies of an anti-microbic immunity only. The serum of patients convalescent from typhoid fever does not contain antitoxic bodies. The interest of the results of Drs. Macfadyen and Rowland's research lies in no small measure in the fact that, by the use of toxins prepared in the manner described, they have obtained a serum possessed of antitoxic as well as anti-microbic properties.

Serum Diagnosis.—As regards agglutination it should, in the first place, be borne in mind that the formation of agglutinins is a process which proceeds simultaneously with the establishment of immunity in the serum of an animal subjected to inoculation. The reaction has been found of enormous value in the diagnosis of cases in clinical practice. It is not an index of the severity of the case, nor of the degree of immunity of the patient's blood. Like the reaction of immunity, it has a high degree of interest, since it may be regarded as a substitute for the experimental reproduction of typhoid fever in animals. The inoculation of animals rapidly brings about the development of agglutinins in the serum. This reaction, which was at first regarded as rigorously specific, has been studied with a view of throwing light on the pathology of typhoid fever. There is general agreement as to its practical utility as a part of the clinical evidence of typhoid infection. Taken by itself it is not absolutely conclusive; but, as Stern (177) points out, the higher the dilution at which the serum agglutinates, the stronger is the evidence in favour of a positive diagnosis. On the other hand, it should be noted that microbic infections other than that of the typhoid bacillus may cause the serum of patients to develop the power of agglutinating (178) the typhoid bacillus at a dilution beyond that which is habitually used in practical methods. The serum from cases of paratyphoid infection, for example, frequently causes agglutination of typhoid bacilli, even though diluted to 1 per cent. It is therefore necessary to regard the evidence as not more than probable. On the other hand, in a series of typhoid cases selected after careful diagnosis by clinical and post-mortem evidence, it is found that the reaction is given in over 90 per cent. Professor Delépine (179), in 1896, estimated the possible error at 2½ per cent, and pointed out that no symptom of typhoid fever is so constant as the serum reaction.

The reaction usually develops after a week or ten days. It may not be given, however, till much later in the disease. The delay in its appearance is one of the chief drawbacks to its practical value. It may

appear very early. The earliest reaction I have seen was in a case which Dr. Tennant worked out in my laboratory. The mother of a small child was one of his typhoid patients. The child, aged five years, also subsequently sickened, and within twenty-four hours of the first symptoms the serum gave a standard reaction. In very slight cases the reaction may sometimes be absent, and, generally speaking, the exact value of the reaction in relation to all forms of typhoid must be considered anew in view of the recent data regarding typhoid infection.

Jürgens (180) points out that we must recognise various groups of cases in which the typhoid bacillus is found in the intestine, and he specifies three of these. (1) The cases in which the bacillus enters and leaves the intestine without multiplication, and the individual remains normal in health. (2) The cases in which the bacillus multiplies in the intestine (181), but does not cause typhoid fever, and does not invade the tissues. (3) The cases in which multiplication takes place, and is followed, or accompanied by typhoid fever.

We are as yet unable to say how the reaction is related to the new definition of typhoid infection, which the most recent work on the subject involves. Since the pathology of forms of infection allied to typhoid fever has been worked out, the specific character of the reaction has been called in question by various authors. In order, however, to understand this question the reader should refer to the detailed account of our present knowledge of the forms of paratyphoid infection (p. 1157). Full accounts of these conditions have been recently published by Bensaude (182), who in 1896 was the first to isolate a paratyphoid bacillus, and by Jürgens (180), who had the opportunity of studying the disease in the Saarbrück epidemic.

Mixed Infection in Enteric Fever.—Considerable importance attaches to the question of mixed infection in enteric fever. Various cases have been recorded in which it was proved that infection with the bacillus typhosus had taken place along with that of another micro-organism, such as, for example, the tubercle bacillus or B. diphtheriæ. Apart from the concomitant infections of this type, invasion by micrococci, or by the bacillus coli communis, has been observed in ordinary cases. Fraenkel showed that pyogenetic cocci occur in the various metastatic forms of inflammation and suppuration met with. While the typhoid bacillus may be found in these foci, it is also recognised that micrococci are frequently the only bacteria that can be discovered in them. This infection arises chiefly, if not exclusively, from the ulcers in the intestine. There is also some evidence that liability to infection from the intestine is increased in typhoid fever. This is due to the regulation of bacterial growth (151) by the bactericidal secretions of the intestine having fallen into abeyance. Direct observations on the bile show that it has lost its normal antiseptic property, and typhoid bacilli are found growing in it. Normal bile, when added to a nutrient medium such as gelatin, in a considerable proportion, *e.g.* 50 per cent, inhibits the growth of B. typhosus and B. coli. In typhoid fever the bacillus typhosus is

abundant in the gall-bladder in nearly every case. Again, Sanarelli has shown that the bacillus coli increases in number and becomes virulent in the intestine in typhoid fever. There are, unfortunately, no corresponding observations on the growth of micrococci in these conditions. Yet there is little doubt that the general mechanism for regulating the growth of bacteria in the intestine breaks down in typhoid fever.

In addition to cases showing local inflammatory foci, there are cases in which the temperature curve shows the remissions associated with general sepsis. In these cases there is, as Wassermann points out, in addition to secondary suppurations, a marked tendency to hæmorrhages in the skin and viscera. Possibly, also, intestinal hæmorrhages may in some cases be due to secondary infections.

The evidence of the invasion of B. coli in typhoid fever is found (*a*) in the frequency with which the blood-serum shows an agglutinating reaction with races of this bacillus; (*b*) in the presence of B. coli in the urine in patients with bacteriuria. This aspect of typhoid infection requires much more investigation.

Epidemiology of Enteric Fever.—Enteric fever is endemic in certain areas, especially in large towns where it causes annually a small proportion of the total number of deaths. In Manchester, the average death-rate during the years 1898-1902, due to enteric fever, was ·4 per 1000 of the population. In Liverpool, during the same period, the average was ·22. In Belfast, on the other hand, the average during this period was ·95, and the reason of the difference was the occurrence there of two epidemics, the first in 1898 and the second in 1901.

To explain the epidemic outbreaks there has been a large amount of investigation on the means by which typhoid infection can be conveyed. Three different forms of explanation have been brought forward.

1. Pettenkofer, to explain the outbreaks in Munich, sought to prove that the variations of the level of the ground-water in the urban area were associated with the rise and fall of the typhoid death-rate. In particular, he tried to show that the fall of the ground-water was accompanied by a rise in the death-rate from this disease. Fodor, however, pointed out that this association was by no means constant, and that in Buda-Pest an increase in the number of deaths from typhoid fever was coincident with a rise in the level of the ground-water (186). Fodor also showed that the relative dirtiness of the houses was a direct index of the susceptibility of the inhabitants to typhoid fever. He found that between 1863 and 1877, of 10,000 inhabitants, there died from typhoid fever, in perfectly clean houses, 162, while in very dirty houses there were 515 deaths.

2. When in 1880-1885 the typhoid bacillus was discovered, it became easy to understand how carelessness regarding the disposal of dejecta from an infected person or persons might lead to an outbreak of epidemic typhoid fever. The conditions under which the bacillus typhosus can exist as a saprophyte were fully investigated with a view to discovering the avenues of typhoid infection. The typhoid

bacillus is, however, singularly elusive, and since it has been demonstrated that though the duodenum is swarming with this bacillus there may still, even with the best methods, be none detected in the fæces, there is no ground for surprise at the failure to discover or follow the typhoid bacillus in various saprophytic conditions. The difficulty has been to a certain extent overcome by adopting as the measure of liability to specific contamination the presence of bacillus coli communis, or bacillus enteritidis sporogenes, or other forms naturally associated with the typhoid bacillus. Such a method at best yields only indirect evidence. The observations on the behaviour of the bacillus itself in external conditions include a study of soil, water, food, and air as vehicles of infection.

Regarding *soil*, it has been found that the bacillus survives only for a short period in soil generally, and in some forms, *e.g.* sand, it dies out very rapidly. Infection is connected chiefly with surface contamination, and the conditions of the survival of the bacillus in the surface layers of the soil, where there is a maximum of fæcal contamination, and a minimum of soil to exercise its purifying influence, have never been thoroughly investigated. Nor, again, do we possess systematic observations on the variations in the bacterial flora of the soil in different conditions (composition, moisture, temperature, etc.). Hence we are still to a great extent in the dark on this aspect of the question.

Water.—The great majority of epidemic outbreaks have been ascribed to contamination of the drinking-water. Schüder (187) has analysed the records of typhoid outbreaks during the last thirty years of the last century. He investigated 650 cases, and found that 70·8 per cent of them were attributed to pollution of the water-supply. It has been shown that the bacillus can survive for some weeks in water if planted there from a culture. Tavel (188) records an instance in which the bacillus had survived in the blind end of a water-main for six months. If the bacillus be sedimented, or incorporated in a mass of protecting substance, it is conceivable, and not at all improbable, that its period of survival may be greatly lengthened.

Milk.—Schüder showed that, in the period he examined, 17 per cent of the cases had been ascribed to milk. The contamination of the milk may arise from impurity in the water used in washing the cans, etc., or may come more directly from the handling of the vessels by infected individuals.

Food.—Other forms of food were found to be responsible for 3·5 per cent of the cases. A conspicuous source from which infection may arise is shell-fish, including oysters.

Air.—The importance of air as an avenue of infection has been remarked upon by those who have investigated typhoid fever in warm countries. There the bacillus may be carried with the dust, or by means of the swarms of flies.

Sanitation.—Liability to typhoid infection has been ascribed to various imperfections in domestic or civic hygiene. I had an excellent oppor-

tunity of testing a number of these points in an investigation on the occurrence of typhoid fever in Belfast, which I carried out for the City Corporation (189). The following is a summary of the observations :—Building houses on foundations consisting of refuse heaps did not increase the liability to typhoid fever in the epidemic outbreaks of 1898 and 1901. The records of the testing of house-drains show that the houses in which typhoid had occurred had, on the whole, better drains than the houses which were free from the disease. The inhabitants of houses on the most dusty streets were not specially liable to typhoid fever during the epidemics. Other points to which the examination was directed were, the state of the sewers, the arrangements for the removal of refuse from the houses, the percentage of imperfectly constructed ashpits, the percentage of privies and water-closets. As far as could be made out, none of these conditions had a predominant influence in originating or maintaining the two epidemics which I investigated.

3. Recently, the work of Koch and the other members of the Trier Commission has drawn attention to the influence of direct infection from one patient to another as the chief means of maintaining typhoid in its endemic form. Koch, in his treatise *Die Bekampfung des Typhus* (1903), shows that typhoid infection may exist in a latent form amongst children and adults, and that the number of cases notified to the public health authority is no measure of the amount of typhoid infection in the members of a given community. In Trier, where eight cases had been notified, a careful search brought the list up to seventy-two, of whom fifty-two were children. In this area, therefore, the number of infected cases was nine times that of the number of cases sufficiently ill to require medical care. In accordance with these results, Koch strongly urges the necessity of isolation and hospital treatment of cases of typhoid infection.

One way of testing the influence of personal infection in the spread of typhoid fever in an epidemic is to work out the proportion of houses which have more than one case. The following table gives the results obtained by this method in my investigation in Belfast :—

	Percentage of Houses with more than One Case.	Total Number of Cases.
Typhoid fever epidemic . .	13·6 per cent	5136 (1898)
Typhoid, moderately quiescent .	7·1 ,,	842 (1903)
Scarlet fever, moderate . .	19·6 ,,	658 (1900)
Diphtheria, quiescent . .	13·2 ,,	321 (1900)

The conclusion from these results tends to show that even in a severe epidemic of 5000 cases typhoid fever has not a marked tendency to spread to other members of the same household.

Fodor has pointed out that in certain years typhoid fever breaks out more or less over large parts of the world, *e.g.* the whole of Europe.

Recently Dr. Chalmers (190) has shown that the towns on the west of Scotland formed, as regards their typhoid death-rate, a group, in the later years of the decennium 1880-90. The towns on the east coast, on the other hand, formed another group in which the rise did not take place. It would be difficult to explain a widespread influence, such as that to which Dr. Chalmers has drawn attention, by the conditions of personal infection.

J. LORRAIN SMITH.

Of **remoter causes** which favour the occurrence of the disease, the following may be mentioned—

1. *Age.*—Enteric fever occurs much more frequently amongst the young and adult persons under thirty-five. It is not uncommon in children, but very rare in infants. This will be evident from some of the tables which accompany this article (p. 1163).

2. *Sex.*—The male sex appears, from the number of cases admitted into hospitals, somewhat more disposed to the disease than females. Thus there were admitted into the Metropolitan Asylum Board Hospitals in the years 1871-1892, 3293 males and 3030 females between the ages of ten and thirty-five years. But probably more males are admitted into hospital than females, so that the susceptibility to enteric fever may be the same in the two sexes, and the liability to infection is probably greater in males (*see also* p. 63).

3. *Season.*—Though enteric fever occurs at all seasons, it is much more prevalent in autumn and the beginning of winter, especially after a dry and hot summer. In London the maximum mortality is in November; in England the maximum prevalence is in October. The seasonal prevalence must be due to some meteorological influence; but the favouring conditions of temperature, atmospheric pressure, and rainfall are not definitely known.

Pathological Anatomy.—We have to distinguish between the lesions which are characteristic of enteric fever, those which are common to most acute febrile infections, and those which are the result of secondary infection or complication.

The characteristic changes are seen in the intestines, mesenteric glands, and spleen.

Intestines.—The lower part of the ileum is the portion affected, and here the parts close to the ileo-cæcal valve are more markedly affected than those higher up. In about one-third of all cases the cæcum and colon show a few lesions, and occasionally they may be met with in the jejunum and even in the duodenum. The affection is to a great extent confined to the lymphoid elements—the solitary follicles and Peyer's patches—and consists, according to Mallory, in a proliferative inflammation followed by ischæmic necrosis, the necrotic tissue becoming separated as a typhoid slough is cast off, leaving an ulcerated surface which undergoes cicatrisation. Considering these several processes more in detail, we have first, and for a few days only, marked hyperæmia of the affected

part, the mucous surface appears swollen and red, and is covered by an abundant secretion of mucus. With the incidence of proliferative changes in the lymphoid elements, the follicles and Peyer's patches become enlarged, and project from the surface of the gut to a distance of 3-5 mm. or more. This, erroneously termed the *stage of infiltration*, reaches its height from the 8th to the 12th day. Microscopic examination shows that the sinuses about the lymphoid follicles are filled with cells of an epithelioid type—the proliferating endothelial cells—many having one large, well-stained nucleus; in others the nucleus is badly stained and pale. They may contain fragments of red corpuscles or leucocytes, thus showing their marked phagocytic character. The blood-vessels may be occluded by fibrinous thrombi; this occlusion is apparently the cause of the subsequent necrotic changes in the hyperplastic tissues; the lymphatic vessels are dilated and filled with cells, and we see in them large ovoid cells with large nuclei. Typhoid bacilli may be seen in numbers in the centre of the follicle where the cell-nuclei appear less stained; they are also collected in large numbers in the lymphatic vessels of the follicle, and a few can be traced into the submucous tissue. When this stage has reached its height (10th-12th day) we may have in mild cases a gradual resolution; the cells which infiltrate the follicular apparatus undergo necrosis or fatty degeneration, and become absorbed. This process may be unaccompanied by ulceration, or by a few superficial erosions only with slight hæmorrhage. In most cases, however, as the swelling of the lymphoid tissue is considerable, the necrosis of the cells (which is a true coagulation-necrosis) leads to the formation of smaller or larger *sloughs*, which are of yellowish or greyish colour, soft, and raised at the edges; these when microscopically examined are found to consist of granular cells, detritus, fibrin, red blood corpuscles, and sundry micro-organisms. The slough gradually becomes detached and an *ulcer* is left (third week of the fever). In cases where the individual follicles of a patch form more or less independent sloughs the effect of their separation is to produce a reticulated appearance—the *plaques gaufrées* of Louis—in other cases the necrotic changes involve the intervening strands of tissue, the slough separates *en masse*, leaving an ulcer which is either round (solitary follicle or partial necrosis of Peyer's patch) or oval (Peyer's patch), with its long axis corresponding to the long axis of the intestine; the floor is usually smooth, and consists of one or other of the intestinal coats—submucous, muscular, or serous—according to the depth of the initial inflammatory process; sometimes the floor is irregular and shreddy, but it is not hardened or much infiltrated; the edges are not indurated, they are often undermined, ragged, and float when the ulcer is held under water. The serous surface of the intestine shows no changes, or is marked by a slight fibrinous deposit.

Microscopic examination of a section of the affected part shows the lymphatic spaces of the intestinal wall adjoining the follicles and floor of the ulcer to be filled with large proliferating endothelial (epithelioid) cells and a few blood corpuscles.

The number of ulcers varies considerably. I have twice seen a solitary ulcer, situated near the cæcum; in ordinary cases they are more numerous near the ileo-cæcal valve, and farther from this site they become smaller and often more shallow.

In a few cases the lesions of enteric fever have been found, with the exception of intestinal ulcers; the Peyer's patches in these cases presented swelling and congestion only. Death in the cases reported had occurred at a date (after the 21st day) when the ulceration ought to have been well marked (94). It may be assumed that in these cases little phagocytic action is opposed to the typhoid bacilli in the walls of the intestines, and that they pass through to the mesenteric glands; or possibly such cases may belong to the group of paratyphoid infections.

Cicatrisation of the ulcer occurs in the last stage; granulation-tissue forms, which gradually become changed into firm fibrous tissue. From the neighbouring part of the mucous surface an epithelial covering extends, and the glands may to some extent become regenerated. The cicatrix scarcely ever tends to narrow the lumen of the gut; it is smooth, depressed, and pigmented, and may be often recognised years after the occurrence of the enteric fever.

Mesenteric Glands.—The anatomical changes in the lymphatic glands are identical with those seen in the intestinal follicles. At first the glands are slightly enlarged by hyperæmia, especially in their peripheral part; then they swell considerably, and become paler and softer (cell-proliferation). The hyperplastic areas then undergo necrosis and become absorbed, and the gland gradually diminishes and becomes firmer. Occasionally the gland may suppurate; this is probably due to a septic infection, though the typhoid bacillus may cause suppuration; the pus may burst into the peritoneal cavity, causing peritonitis, or it may become inspissated, and eventually infiltrated with lime salts. A man, who two years before had passed through a severe attack of enteric fever, came under my care for symptoms pointing to obstruction of the small intestine, and an operation was performed: the cause of obstruction was then found to be a large mesenteric gland which had become adherent to a part of the small intestine, and by dragging on a portion of its wall had caused marked diminution of the lumen.

The *spleen* also shows similar changes. It gradually increases in volume, and by the end of the third week may be three to four times its normal size and weight; the swelling is less marked in old people. During the first week there is hyperæmia. The capsule becomes stretched, and on section the spleen has a dark-red colour, and the stroma is indistinct; gradually the pulp becomes softer, diffluent, and the Malpighian bodies appear distinct and larger (third week); with the fourth week, or sometimes later, diminution begins, the pulp appears pale or brownish, the consistence of the spleen becomes increased, and later still the stroma becomes more fibrous. Histologically we find at the height of the disease an infiltration of leucocytes, some of them degenerated, large endothelial cells with one or more nuclei, and large cells containing several red blood

corpuscles. The typhoid bacilli are found disseminated through the spleen, and are often found in clumps.

The *tonsils* and the glands in the pharynx are enlarged and infiltrated, but as this is seen in other acute infective fevers, it cannot be looked upon as a lesion specific to enteric fever.

The *bone-marrow* presents lesions very similar to those met with in the lymphatic elements. Congestion, œdema, focal necrosis, the presence of many large phagocytic cells, and more or less hyperplasia of the lymphoid follicles are the characteristic changes (Longcope). The typhoid bacillus has been repeatedly demonstrated in the bone-marrow, and appears to have some relation to the focal necroses.

I will now briefly touch upon the lesions found in the other organs in enteric fever, omitting those affections the nature and appearance of which is sufficiently evident during life, and a description of which will be found under Symptomatology.

Digestive Tract.—Ulceration of the pharynx, possibly of specific origin, arising in the lymphoid elements has been noted. In the œsophagus ulceration occasionally occurs, here it is probably of a secondary origin; in a few cases the healing of such ulcers has produced stenosis. The stomach is often the seat of catarrh. Cornil describes cell infiltration of the adenoid tissue, and compares it to the intestinal lesion. Dr. Handford noticed similar changes and hæmorrhages. The solitary follicles of the *cæcum* and *colon* participate in the specific changes in about one-third of all cases. There may be ulceration also of the appendix; the rest of the large intestine is often the seat of catarrh, and occasionally ulcers are noticed, which may go on to perforation, which is less serious than perforation of the small intestines; perforation of the rectum has been found with formation of a recto-vaginal fistula. I have once seen marked hæmorrhagic infiltration of the greater part of the large intestine. The *liver* is not found enlarged except in the early stages of the disease; it is pale in colour, flabby and somewhat friable, the normal lobulation being indistinct or quite obliterated. Histologically we find more or less marked albuminous and fatty degeneration of the liver-cells, and scattered focal lesions which, according to Mallory, are of two kinds, one consisting of accumulations of epithelioid cells in the lymphatic spaces and vessels about the portal vessels, the other of small areas of necrosed liver-cells associated with and apparently secondary to occlusion of the adjacent capillaries by similar epithelioid cells. The capillaries are sometimes dilated, and when death has taken place at a late period of the fever we find slight perilobular cell infiltration in the portal canals. Typhoid bacilli are often seen in large numbers filling up the capillaries (75).

Acute yellow atrophy is a very rare complication. Hepatic abscess is occasionally met with; it is invariably due to secondary infection with pyogenetic cocci, and it may result from infection through the hepatic artery when there is a complicating general pyæmia, from infection through the portal vein—pylephlebitis—from some focus of suppuration

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in the intestine or appendix, or, lastly, from the direct extension of some suppurative process already existing in the gall-bladder or large bile-ducts. The gall-bladder and large bile-ducts may be the seat of catarrh; suppuration, ulceration, and perforation of the gall-bladder are rarer. Gallstone formation is an important and not very uncommon sequel of typhoid fever. The bile in the absence of biliary lesions is light coloured and limpid, and as it contains almost constantly the typhoid bacillus in a virulent form, it appears obvious that it must have undergone some change in composition whereby its antiseptic character has been lost (*vide* p. 1094).

The spleen may be the seat of infarcts which may form pyæmic abscesses; in persons who have died after many weeks from exhaustion owing to long-continued suppuration (bed-sores, empyema), lardaceous change may be found in the spleen and other organs.

Lungs.—Besides the affections mentioned under symptoms, there may be hæmorrhagic infarcts and occasionally gangrene or pyæmic abscesses in the lungs.

Heart.—The heart is flabby, pale in colour, and soft in consistency, sometimes almost friable. Microscopic examination reveals a variety of changes; in some cases no noteworthy alteration in the myocardium is found, in others there are changes in the muscular fibres, interstitial tissue, and blood-vessels. The muscular fibres may show fatty degeneration and occasional waxy degeneration; in some cases of sudden death segmentation of the muscular elements (*myocardite segmentaire* of Renault) has been noted, a change regarded by many as being of agonal origin; in cases in which the fever has run a more protracted course, small pigment granules in the neighbourhood of the muscle-nuclei have been observed; hyaline (Zenker's) degeneration is rare; intermuscular cell infiltration is occasionally seen, and the small arteries of the myocardium may be the seat of endarteritis of an obliterating type (108); according to Hayem this is especially prevalent in cases which have terminated suddenly. Chantemesse and Widal have found typhoid bacilli in the heart-muscle. The *endocardium* and *pericardium* are not often affected, though occasionally there may be both the vegetative and ulcerative form of endocarditis; the lesion is due in many cases to pyogenetic organisms, but in several the typhoid bacillus has been isolated in pure culture from the affected valve. In the aorta Potain has met with a condition of acute aortitis. Thayer (127A) has brought forward evidence to show that arteriosclerosis is more frequent in persons who have had enteric fever in the past than in those who have not.

The Kidneys.—The changes in the kidney are manifold, and are not always in proportion to the renal symptoms exhibited during the disease. In some instances in which there was persistent albuminuria with casts, no noteworthy changes have been found; but in most cases, even with but slight albuminuria, there is cloudy swelling of the epithelium of the convoluted tubes; in cases in which during life there have been signs of hæmorrhagic nephritis, or in which from the first there have been grave

renal symptoms, the changes are marked. The kidneys are enlarged, especially the cortical part, and the epithelium of the convoluted tubes is granular. Renault describes a distension of the glomerular cavities and adjacent renal tubes with albuminous material. Perivascular cell infiltration may also be noticed. In cases with septic complications there are sometimes small-cell accumulations round the blood-vessels in various parts of the kidney. These have been specially noticed by Wagner, and have been compared to multiple lymphomata; they represent, however, only microscopic abscesses, and may eventually lead to small visible abscesses. They are found more often in scarlet fever and diphtheria than in enteric fever. The typhoid bacillus and B. coli have both been found in sections of the kidney.

Muscles.—Though perhaps more frequently found in enteric fever, the changes observed here have been noticed in other febrile affections. Some of the muscles (recti abdominis, adductors of the thigh, pectorals, diaphragm) appear pale and waxy to the naked eye, and microscopically examined show Zenker's hyaline degeneration. A muscle so affected may rupture and give rise to hæmorrhagic extravasation. Other muscles show fatty degeneration, especially when fever has continued for weeks. Another change consists in a proliferation of the muscle-nuclei. According to Metchnikoff, this appearance is due to an infiltration with leucocytes (phagocytes) rather than to a nuclear proliferation.

Nervous System.—Most of the nervous symptoms during the fever are due to the specific intoxication, and have no definite morbid anatomy; yet certain alterations have been found, such as œdema of the membranes and of the brain itself and distension of the ventricles, pigmentation of the ganglion-cells, infiltration of the perivascular spaces with leucocytes, and of the spaces round ganglion-cells, fatty degeneration of nerve-fibres, and hæmorrhages (meningeal and cortical). (See also Symptomatology.)

Symptomatology.—The symptoms of enteric fever vary considerably in individual cases both as regards character and intensity; this is due partly to the intensity and localisation of the poison, and partly to a mixed infection. It will be well to describe at first an ordinary case, then to give an analysis of the symptoms, of the complications, and of the sequels. In each case of enteric fever we may take certain periods to represent the several stages of the affection. The following stages are recognised by most clinicians: incubation; onset or invasion; the fever period itself, which is divided into the first, second, and third week of the fever—or, according to Murchison, into the stage of glandular enlargements extending to the 12th or 14th day, the stage of ulceration or sloughing of the intestinal glands extending to the end of the third week; lysis or gradual diminution of the fever, and convalescence.

The *incubation period* varies considerably; it seems in most cases to be about fourteen days; in some cases, however, it has been ascertained to be as short as four or five days, or even less; in the case of a patient who, with suicidal intent, swallowed a virulent culture of typhoid bacilli, it was three days (Dufloeq and Voisin); in others it may extend over

three or four weeks. During the period the patient may either experience no symptoms whatever (5 to 10 per cent), or, as is most commonly the case, towards the end of this period, he may complain of headache, loss of appetite, sleeplessness, and a sense of fatigue; this stage may gradually pass into the next stage.

The Onset.—In many ordinary cases the onset is insidious. The patient complains of pain in the limbs, of excessive fatigue, of cold and chilly sensations, of headache often very severe, of loss of appetite, of abdominal pain, of diarrhœa, and of sleeplessness: epistaxis is very common, much commoner in my experience than the recent statistics of Prof. Osler would indicate (182 out of 829 cases); it generally occurs about the second or third day of the disease. These symptoms become more severe, the patient has to take to his bed, and from this day we generally reckon the duration of the fever. In many cases, however, as shown by the changes after death, the beginning of the morbid process must be dated from the very first symptom. The tongue becomes furred, and is at first moist; there is a steady rise of temperature, the evening temperature being generally one and a half degrees (F.) higher than the morning temperature, so that at about the fourth day it reaches 103° or 104° F.; the pulse rises to 90 or 100, rarely higher except in very severe cases, or in very young or debilitated subjects, is dicrotic and indicative of low blood-pressure; there is increased thirst; the abdomen is slightly distended and tender on pressure; diarrhœa may as yet be absent, and there may be constipation, or there may be two or three fluid stools from the first. Some patients have a short, dry cough and occasionally complain of dyspnœa. Beyond the headache, which persists for a few days, and sleeplessness, there are as yet no other symptoms; the skin is dry, but there are paroxysms of profuse perspiration. The spleen is as yet but little enlarged, and there are no rose-spots, though when perspiration is profuse sudamina are noticed; the urine has febrile characters and as yet does not show the diazo reaction. This stage lasts about seven days, and constitutes the first week of enteric fever.

During *the second week* more characteristic symptoms appear. The fever remains high and steady, the morning remissions being less; the pulse is quicker; the skin remains moist; the tongue becomes dry and brown, and the lips likewise; the roseolar rash appears between the seventh and twelfth day, in the case of Dufloeq and Voisin it appeared on the 5th day; it consists of isolated, circular, rose-coloured, slightly elevated flattened papules, from two to four millimetres in diameter, disappearing on pressure, and reappearing with the removal of the pressure; they occur chiefly on the abdomen and back, occasionally on the arms and thighs, rarely on the face; they may be very few in number, or at times very numerous, and they appear in successive crops, persist from three to five, occasionally ten days, and then gradually fade, leaving a brownish stain: the spots continue to come out up to the end of the second week, and often to the middle or end of the third week, or even during convalescence. In explanation of the distribution of rose-spots

over the abdomen and lower thoracic zone, Dr. Greenhalgh points out that this cutaneous area is in direct association through the nervous system with the foci of disease, namely, the small intestine, its lymphatic glands, and the spleen; that here there exists a reflex inhibition of the vaso-constrictor impulses, and consequently an abnormal facility for the lodgment of clumps of agglutinated bacilli, which by irritation produce a local inflammatory reaction, manifested as a circular, raised rose-spot. With the subsequent action of bacteriolytic substances in the blood-serum and the destruction of the bacilli the rose-spot subsides. In some cases a minute vesicle may be seen at the apex of the roseolar spot. During this stage the abdomen becomes more distended, gurgling in the right iliac fossa is noticed, and the abdomen may be painful on pressure. The diarrhœa is now more profuse, and the motions have the characteristic pale yellow ("pea-soup") colour, and, especially in children, are highly offensive. The spleen is now considerably enlarged, is often to be felt below the costal margin, and is occasionally painful on pressure. The respiration is quickened, but not to the same degree as in pneumonia; still there may be some bronchial affection with mucous expectoration. The temperature during the first few days of the second week continues high, with marked evening exacerbations. About the middle of the second week, in moderately severe cases, the morning temperature is lower than it was before; in others the morning remission is but slight, and the fever has a less remittent character; in very mild cases the fever may disappear about the end of the second week. The urine is scanty, high coloured, and of high specific gravity; occasionally it contains albumin, and in most cases gives the "diazo-reaction." The headache usually disappears during the second week if not before, and there is often marked and increasing deafness. The patient in the second week, except in very slight cases, assumes a somewhat characteristic appearance. He is dull, apathetic, and has a heavy look; the face is pale, the cheeks occasionally flush, the pupils dilate, and the lips are dry. In severer cases there is delirium, especially at night, and in still more severe cases other nervous symptoms (constant delirium, somnolence, subsultus tendinum) may supervene, and death may take place during the second week. Hæmorrhage from the bowel or perforation occasionally occurs towards the end of the second week.

During *the third week*, in mild cases, the symptoms gradually subside. In moderately severe cases most symptoms remain the same as during the second week; but the temperature shows marked morning remissions, and the fever gradually declines, and may show for a few days an intermittent type,—the morning temperature being normal, the evening temperature still reaching 100° or 101° F.; in more severe cases the temperature may remain high and even increase, the pulse becomes smaller and quicker, the tongue quite dry, brown, and often fissured, the lips covered with sordes, the diarrhœa persistent, and the perspiration profuse: the delirium is now constant, and often of a low, muttering, or sometimes of a violent maniacal character; the loss of flesh

becomes particularly apparent during this week, and bed-sores may appear if the nursing be inefficient. Hæmorrhage from and perforation of the intestines are apt to occur during this week. Pulmonary complications and failure of the heart's action are to be feared, and would show themselves by quick and small pulse, cyanosis of the face, clammy perspiration, and the like; other unfavourable symptoms relating to the nervous system may also occur towards the end of the third week, such as retention of urine, or involuntary discharge of urine and fæces.

With the *fourth week* convalescence commences in ordinary cases, in very severe cases later. The evening temperature now falls gradually to the normal, or nearly so; save in a few exceptions (Fagge, Morris) there is no crisis, but a gradual defervescence; the alvine evacuations become formed, the pulse improves, and the tongue begins to clean, while the appetite returns and becomes almost ravenous; the pulse becomes slower and firmer; there is often polyuria, the urine having a low specific gravity; the nervous symptoms quickly disappear; the sleep becomes more natural, and though the patient feels excessively weak, often complains of vertigo and palpitation, and is pale and anæmic, the strength gradually returns and is maintained; unless the convalescence be interrupted by *relapses*, or some of the sequels to be mentioned below ensue. In very severe cases the fourth week often brings not only no relief, but even an aggravation of the symptoms of the third: the pulse may reach 140 or more, the respirations become laboured, the face is dusky and covered by clammy perspiration, urine and fæces pass involuntarily, and coma gradually sets in, soon followed by death: some few patients, however, in spite of the severity of the symptoms, take a favourable turn, and eventually recover. Convalescence begins in the majority of cases with the fourth week: in not a few cases, however, the fever does not subside till the end of the fourth week; whilst in some protracted cases it may continue during the fifth or even the sixth week.

The above is a brief description of the symptoms in ordinary cases of enteric fever. Certain variations, both in the onset and course of the disease are, however, sometimes noticed.

As regards the *onset*, it is well to know that occasionally this may be sudden, in one of the following ways—(*a*) Symptoms resembling an ordinary febrile cold: repeated shivers, with headache and rise of temperature; but a single rigor, so characteristic of pneumonia, is rarely seen in enteric fever. (*b*) Symptoms resembling acute gastritis: such as frequent vomiting, which may persist for a few days, and be soon followed by diarrhœa; the gradual increase of the temperature, which on the fourth day may reach 103° or more, assists us in diagnosing such a case from gastro-intestinal catarrh. (*c*) In other cases the patient at first complains of sore throat, and the tonsils may be so swollen as to interfere with breathing and swallowing; the accompanying headache, epistaxis, and pyrexia here assist us to make an early diagnosis. (*d*) The first symptoms may be those of pneumonia, and only after some days the typhoid symptoms (diarrhœa, enlargement of spleen, roseola) present

themselves. These cases are known as pneumo-typhoid, and, as in some of them the typhoid bacillus has been found in the pneumonic lung, the condition is probably, in some of the cases at least, enteric fever in which the typhoid bacillus established itself first in the lungs; in other cases we probably have to do with two coincident affections—pneumonia and enteric fever (Chantemesse). (*e*) The fever may set in with severe facial neuralgia persisting for several days, or, as in a case which I recently saw, with stiffness in the muscles of the neck. In this instance the stiffness occurred for several days with each exacerbation of temperature, and lasted several hours; beyond the pyrexia there was no other symptoms of typhoid; yet both the diazo-reaction and the agglutination reaction were positive. In other cases, again, there are severe headache and vomiting, soon followed by delirium, retraction of the head, and photophobia—indeed all the symptoms of meningitis; and it is only after five to six days that the true nature of the case reveals itself; this onset is not rare in children. In other cases the symptoms are those of basal meningitis; or, lastly, the onset of the fever may be characterised by mania. (*f*) Symptoms of acute nephritis (nephro-typhoid) (see p. 1125). (*g*) In very rare cases laryngeal symptoms (laryngo-typhoid, p. 1114).

During the stage of glandular enlargement the temperature may not show the characteristic curve; it may be normal, or but little above normal, throughout the whole course (apyrexial type), or slightly febrile (in mild cases), or it may show great variations; again, diarrhœa may be absent throughout the whole course, or there may even be obstinate constipation. Grave nervous symptoms may persist throughout the whole period, as in the form of constant delirium or drowsiness; the presence of the other symptoms characteristic of the disease helps us in the recognition of these aberrancies. As the symptoms vary considerably in some cases, I will now give a brief analysis of the symptoms relating to the various organs.

Temperature in Typhoid.—For the majority of cases the observations of Wunderlich on the temperature-curve in enteric fever still hold good. With the onset the temperature rises gradually during the first four days, an evening exacerbation of about 1·5° to 2° F. being followed by a remission next morning of about 1° F., so that there is a gradual mean rise with a daily zig-zag, the summit of which reaches about 103·5° to 104° on the fourth day. This is followed by the fastigium, lasting for about seven days, during which time the temperature is more uniform and of continuous type, the morning temperature being 102° to 103°, evening temperature 103° to 104° F. In many cases there is on the seventh day a distinct but only temporary fall of a few degrees. From this point to the end the temperature varies with the severity of the case (excluding such accidents as hæmorrhage); in ordinary moderately severe cases the temperature, after the eleventh or twelfth day, has for three to four days a remittent character, the morning temperature now falling, and more rapidly than the evening temperature; during the remaining days (from about the sixteenth to the twenty-first) it assumes

an intermittent character, the morning temperature being about normal, the evening temperature reaching 101·5° to 101° F., and coming somewhat rapidly down to the normal on the twenty-first day: in mild cases the temperature may fall more rapidly at the end of the second week, and may reach the normal soon after; in severe cases the morning temperature remains high after the second week, between 103° and 104°, and the evening temperature reaches 105° F.; or we have irregular temperatures for several days after the twelfth day (the "amphibolic stage" of Wunderlich, the "stage of changing fortunes" of Murchison). Defervescence thus takes place more or less gradually; but sometimes the fever may terminate by sudden crisis on or before the end of the third week. For the majority of cases, then, Wunderlich's observations on the temperature hold good, and from a diagnostic point of view it is well to remember his general rule:—Any fever which on the second day reaches to 104° F. is not enteric fever, nor is it enteric if the fever does not approach 104° F. on the evening of the fourth day; on the other hand, enteric fever may be diagnosed if in a middle-aged person suffering from an acute febrile attack the evening temperature on the fifth day, or within the first week, is between 103° and 105°, and alternates with morning temperatures, which are 1·4° to 1·7° lower, unless some other disorder can be discovered to explain the height of the fever. It is well to state that by morning temperature we mean the temperature about 9 A.M., by evening temperature that about 6 P.M. If the temperature be taken every two hours greater differences are sometimes noticed during the twenty-four hours; not uncommonly two, rarely more, distinct elevations of temperature occur, one generally about mid-day. This feature may persist throughout the entire fastigium.

There are, however, many variations of the temperature-curve. Chills may be met with under a variety of conditions—(1) with the fever of onset; (2) occasionally throughout the course of the disease, followed by profuse sweats (sudoral form); (3) with the advent of complications; (4) with active antipyretic treatment with benzene derivatives; (5) occasionally during defervescence, without relation to any complication or sequel and probably due to septic infection; (6) from constipation; and (7) in certain cases during the latter half of the disease (90). Sometimes, especially if pneumonia intervene, or even in simple cases, there may be a very high temperature on the second day; again, we occasionally meet with hyperpyrexia, which may reach 109° and even 110° F. Such temperatures generally occur during the third week, and are quickly fatal; but temperatures between 105° and 106° F. may be met with even towards the end of the second week in cases which recover, especially in young subjects. Again, the temperature may undergo sudden alterations from incidents which arise during the fever; thus an attack of pneumonia, occurring, as it often does, towards the end of the fever, causes a sudden rise of temperature; various septic affections, which so often complicate enteric fever, considerably disturb the fever curve; hæmorrhage from the ulcers causes a sudden fall of the temperature;

perforation of the bowel often has a similar effect; and even nervous symptoms, or failure of the heart, may be ushered in by a fall. Oscillation between high and very low temperatures may occur; thus in a child suffering from enteric fever the temperature fell from 104° to 91° F., and then gradually rose to normal. With the rapid fall of temperature signs of pneumonia appeared (100). The anæmia following severe hæmorrhage is occasionally associated with marked oscillations of temperature (Osler). Again, the fever, instead of terminating at the end of the third or fourth week, may run on for weeks, protracted by a variety of causes, such as continued ulcerations, septic complications, etc. The temperature may exhibit an inverted type in persons whose occupation is nocturnal, as bakers, policemen; and occasionally in the aged and in children.

Some cases of enteric fever may run their whole course without any rise of temperature, or with a temperature but slightly above normal, or even with a subnormal temperature. Such cases have been described by Gerhardt (50, 135) and myself (28). Even epidemics of such cases have been described (43). In two of the cases observed by me, not only were all the prominent symptoms of enteric fever present, with the exception of pyrexia, but there was also a distinct relapse, lasting in one case exactly three weeks, during which there was marked hæmorrhage from the intestines. The prognosis of these cases, in spite of their apyrexial nature, is as grave as that of ordinary enteric fever; one of my patients died from perforation, and the two cases described by Wendland terminated fatally.

Post-Typhoid Pyrexia.—Apart from the cases mentioned above, in which the temperature, on account of some complication or continued ulceration, does not come to the normal for many weeks, we may note a rise of temperature lasting a short time; this occasionally happens during convalescence, and is sometimes referred to excitement, errors in diet, or too nitrogenous a diet, or to constipation (in one case the temperature ran to 105° F. after having been normal for three days, and quickly subsided again after an enema). Slight elevations of temperature during convalescence are often noticed in children, in very anæmic persons, or in those of highly nervous temperament; on the other hand there may be persistent hypothermia for ten days or more in protracted cases with great emaciation, which, however, has no special significance (Osler). From these post-typhoid temperatures must be distinguished the fever of the relapse, which will be described hereafter.

Signs on the Surface of the Body.—The roseolar eruption has already been described. It is present in about 77 per cent of the cases (in 85 per cent of Professor Osler's 829 cases); it is more often wanting in children, but may be even copious in them. Among other eruptions met with are:—

(*a*) Maculæ cæruleæ, tâches bleuâtres, peliomata, blue-tinted spots of indefinite size, situated chiefly over the chest, abdomen, and thighs; these appear to be caused by the irritation of pediculi, and occur in other febrile affections.

(*b*) Petechiæ or purpuric spots.—In rare cases the typical typhoid rash may be accompanied by petechiæ; at other times, in badly nourished and debilitated persons, or when septic complications occur, petechiæ may appear at the height of the disease.

(*c*) Miliaria and sudamina are not unfrequently met with; they appear sometimes early, but generally in the second and third week of the disease; they are very numerous, and are principally on the front and back of the chest and on the abdomen; the sudamina are small vesicles, filled with clear fluid, and are not likely to be mistaken for any other affection. This eruption, of course, occurs in many other diseases.

(*d*) Erythema.—A rash of vivid red colour, not unlike the scarlet fever rash, sometimes appears during the first week, chiefly on the chest and abdomen. I have twice noticed a similar rash occurring during the third week, and chiefly affecting the arms. This rash may in some cases be due to the administration of drugs—quinine, salicylate of sodium, antipyrin, etc. It has been observed, however, quite independently of such drugs (87, 140), and is probably of septic origin.

(*e*) Morbilliform rash, resembling measles (77, 89), in larger or smaller patches, with a dark hæmorrhagic centre and a lighter coloured periphery, affects the neck and trunk, spreads rapidly, but does not extend to the mucous membrane, and appears not materially to affect the course of the fever. Neumann found the streptococcus pyogenes on the arms of a patient during the existence of this rash.

(*f*) Urticaria is occasionally observed, but is probably in most cases a drug eruption.

(*g*) Herpes, so common in pneumonia, is rare in enteric fever; it has been observed sometimes, however, during the first week. In two cases in which I noticed it the enteric fever was complicated by pneumonia.

(*h*) Desquamation in fine branny scales is often observed towards the end of the fever or during convalescence, and especially in children.

Œdema of the skin is sometimes noticed towards the end of the febrile period (from thrombosis of a vein), or during convalescence (from anæmia and nephritis).

Erysipelas is occasionally noticed as a complication. I have seen it twice in children; it occurred when the febrile symptoms were subsiding. It commenced in the usual way—the face, forehead, and ears being chiefly affected, and it ran a favourable course. Silvestrini, in a case of erysipelas complicating enteric fever, found the typhoid bacillus in the erysipelatous eruption.

Boils are not an uncommon sequel; they appear to be more frequent after the use of cold baths.

Bed-Sores.—The marked improvement which has taken place in the nursing and management of fever patients has almost banished bedsores; yet in a few very protracted cases in very debilitated persons, whatever the precautionary measures, they may perhaps be unavoidable;

and several factors, besides mechanical pressure—such as the condition of the blood, and trophic changes due to central nervous causes—help in their production. They are noticed over the sacrum, or over the trochanters, knees, elbows, ankles, shoulders, head, and elsewhere. At first the skin reddens, then small superficial erosions or fissures appear, and these deepen, giving rise to gangrenous patches, which may slough off, leaving the subjacent parts bare; occasionally the destruction of tissue extends, and may be accompanied by suppuration and the appearance of septic symptoms. We may thus have extensive destruction of bone, which, when it affects the sacrum, may lead to septic meningitis, or when the bed-sore is situated over a joint may lead to opening of the articular cavity and further changes.

Circumscribed gangrene of the skin is an occasional complication seen in greatly debilitated individuals.

During convalescence there is occasionally *loss of hair*, which, however, in most cases grows again. As in other fevers and severe diseases, a transverse *ridging of the nails*, from interference with nutrition, is noticed after recovery from enteric fever. There is an opaque white line, followed usually at some little distance by a depression; starting close to the bed of the nail; gradually with the growth of the nail it advances forward till eventually it disappears; in older people, however, it may remain visible for a long time.

Atrophic striæ may appear on the skin of the abdomen, on the lateral aspects of the thighs, over the patellæ, and elsewhere. They have been regarded as of neurotrophic origin.

The circulatory system presents important symptoms, especially from a prognostic point of view. As in other febrile infectious diseases, the continued high temperature, the toxic products of the micro-organism, and the presence of the typhoid bacilli in the myocardium (Chantemesse), and especially also secondary infection, exert a deleterious effect on the heart-muscle (typhoid myocarditis), and are often the cause of death in typhoid; the blood itself presents important changes which differ somewhat from those seen in other acute febrile affections, and lead to further disturbances, especially in the post-febrile period.

Pulse.—During the first week, and during the whole period of the fever in cases which are likely to end in recovery, the pulse, except in children, ranges from 86 to 100 in men, and from 100 to 120 in women; it is distinctly and markedly dicrotic, indicating a paresis of the arterial muscular coat and low blood-pressure. The force of the pulse varies, of course, with the age and strength of the individual and the condition of the heart; according to Potain, the blood-pressure in the arteries is always diminished (see on this subject also Moser (88)). During the second and third week the pulse generally becomes a little quicker and less dicrotic, and during convalescence may be very slow. A small and quick pulse is of bad omen; Liebermeister found that when the pulse reached 140 pulsations per minute death occurred in 50 per cent, and when over 140 the mortality was 80 per cent. The prognosis is equally

unfavourable when the pulse becomes irregular and intermittent, even if not very frequent; such a pulse is often followed by pulmonary or cerebral thrombosis, with sudden death at a later period, and indicates myocarditic changes. In some cases of enteric fever a slow pulse (50-40) has been noticed throughout the disease, which returned to its normal frequency during convalesence (Murchison). There is no definite relation between the temperature and the pulse, though often with a rise of temperature the pulse-rate increases.

Myocarditis.—Manifestations of the inflammatory changes in the heart-muscle are likely to occur at the end of the second or the beginning of the third week.

In ordinary uncomplicated cases physical examination reveals nothing abnormal; in severe cases the first sound may be very feeble or quite inaudible, as pointed out by Stokes; or the first and second sound become very similar in timbre and duration (embryocardia); sometimes a systolic murmur is heard at the apex or over the area of the pulmonary artery. With these signs dilatation of the heart, cyanosis, and venous pulsation may be noted. French observers have described a cardiac form of enteric fever. These cases are characterised from the first by quick, small, and irregular pulse, a low temperature, pallor of the face and extremities, and retrosternal pain. The prognosis of these cases is always very grave, and death often occurs from collapse or syncope.

Pericarditis and endocarditis are rarely observed in typhoid fever, and are of less importance.

Arterial Thrombosis.—As further complications, especially during the last stage of and during convalescence from typhoid, blocking of arteries and of veins may occur. A probably specific affection of the arteries, a typhoid arteritis, has been described by French observers. This affection, if it occur, is almost always met with during convalescence; it affects the large trunks, is associated with thrombosis, and is ushered in by fever and by pain over the affected artery, which can be felt as a cord-like mass; the pulse in the vessels below the obstruction is very much diminished, œdema appears in the peripheral part of the affected limb, and in some cases dry gangrene follows: the surface temperature of the affected part is most usually diminished. In a case reported by Dr. Sydney Phillips, in which blocking of the left common femoral artery took place, the surface temperature of the affected limb showed an increase of 5° F. Keen (64) has collected 115 cases of gangrene in typhoid fever, due to arterial thrombosis or embolism. In the lower extremities it occurred with equal frequency on the two sides. The obliterating visceral arteritis described by Landouzy and Siredey is of little importance.

Thrombosis of veins is much more frequent. It occurs during the third week or later. It affects most commonly the left femoral vein, but may involve other veins, as of the upper extremity; it is ushered in by slight rise of temperature, occasionally (28 per cent) preceded by a chill, severe local pain, often lasting several days, marked swelling of the limb,

œdema, and leucocytosis; occasionally several attacks of thrombosis may occur during convalescence. In one case under my own observation each attack was preceded by a rigor, very high temperature, very quick pulse, and profuse sweating. In the clot obstructing the vein micro-organisms have been found (Vaquez). The thrombosis may extend into other veins; it may lead to pyæmic symptoms, and sometimes causes sudden death from pulmonary embolism. If by the thrombosis of the vein the adjacent artery be much compressed, or if clotting in the artery be associated with it, gangrene of the distal part of the limb ensues.

Embolic infarcts of the spleen, kidney, and lungs are sometimes seen post-mortem. Unless these infarcts are very extensive, they cannot often be diagnosed during life.

The *blood* in enteric fever shows some marked changes (127). The number of red blood-corpuscles, normal at first, falls progressively during the febrile period, and even into the afebrile period, the average loss being about 1,000,000 per c.mm. During convalescence, usually from two to three weeks after defervescence, the number gradually returns to the normal. With the onset of relapses the number of red corpuscles is often smaller than during the initial febrile period. The red blood-corpuscles may undergo apparent changes in number during the fever; thus profuse diarrhœa or sweating may cause a temporary increase, hæmorrhage a decrease. The amount of hæmoglobin falls and rises with the number of the red blood-cells. The number of leucocytes in the peripheral circulation is subnormal throughout the febrile period, varying from 9000 to 2000 per c.mm. in uncomplicated cases. Exacerbations may be associated with a further reduction of a 1000. Counts above 10,000 are rare, and usually indicate the incidence of some complication or the effect of some extraneous influence—a marked difference between enteric fever and inflammatory affections and most infectious fevers. Some observers, however, have noticed a slight increase at the beginning of the attack. Differential counts show that it is the polymorphonuclear neutrophils that are chiefly reduced, the percentage falling on an average to 60, and not rarely below 50. The large mononuclear leucocytes are relatively increased. The eosinophils are reduced to below 1 per cent. A leucocytosis, which brings the number of leucocytes to the normal or above, occurs in inflammatory complications, within a few hours of an intestinal perforation, and usually after an intestinal hæmorrhage. An immediate and transient increase may be observed after a cold bath; in very severe cases of typhoid leucocytosis may not occur. With convalescence the number gradually returns to the normal. Eichhorst found in one case large granular cells containing several red blood-corpuscles. The specific gravity of the blood taken after the method of Schmelz shows considerable diversity. The glycogen of the blood has been found increased. Drs. Wright and Knapp found that the coagulability of the blood was diminished during the febrile period, and was higher than normal during convalescence. Typhoid bacilli have been found in blood

drawn from the spleen, from a superficial vein, and from the roseolar eruption in a large proportion of the cases examined (see p. 1087), and it is probable that they are present in the blood in every case during some stages of the disease ["Typhoid Septicæmia"]. Streptococci and staphylococci have been found in the blood in mixed infection.

Respiratory System.—Epistaxis as an early symptom has already been mentioned. Occasionally it is very profuse, and in the hæmorrhagic typhoid it is a prominent feature. The nasal mucous membrane is dry, red, and swollen, and occasionally presents superficial erosions and submucous suggillations.

Laryngeal affections are not uncommon, though there is much diversity of opinion as to the proportion of cases affected. In many instances there are no subjective symptoms, and the nature and extent of the affection are only shown by laryngoscopic examination; in others the symptoms are dryness and tickling of the throat, hoarseness, cough; while some affections, like œdema and perichondritis, may give rise to alarming and sometimes quickly fatal symptoms. The various affections are—

1. Catarrhal Laryngitis.—A mild form, little more than a simple hyperæmia of the mucous membrane, is of frequent occurrence; the more severe forms are much less common.

2. Ulcerations may arise as a result of inflammatory changes in the lymphoid elements of the larynx; they are analogous to the specific intestinal lesions, and like them are due to the typhoid bacillus. Such cases with pronounced laryngeal lesions would by some be designated "laryngo-typhoid." These ulcerations are situated in the parts of the larynx provided with lymphoid follicles, namely, the base of the epiglottis, the posterior wall of the larynx, especially the inner surface of the arytenoid cartilages, and the posterior attachment of the vocal cords. These ulcers may be simple erosions and heal readily, or they may become necrotic and leave sharply defined defects, or they may lead to extensive perichondritis and exfoliation of the cartilages. Typhoid bacilli have been found in these follicles by Schultz.

3. Ulcerations, especially those situated on the posterior wall of the larynx, may arise in superficial erosions and fissures in the mucous membrane which have become secondarily infected by streptococci and staphylococci (Eppinger, Landgraf). They appear at first in the form of yellowish spots, which break up into smaller masses. These masses slough and become detached, leaving more or less deep ulcers, which may lead to further changes.

4. True Diphtheritic Laryngitis.—This is extremely rare, and but few undoubted cases (50) are recorded (compare p. 990). In one case the diphtheritic membranes extended to the bronchi, and the soft palate was also affected.

5. Perichondritis with exfoliation of the cartilages, which may lead to marked narrowing of the larynx, or in rare cases to subcutaneous emphysema of the neck, must in nearly all cases be looked upon as

secondary to the ulceration. Some authors assert that perichondritis may arise without previous ulceration of the mucous membrane, the condition being analogous to a specific periostitis of the long bones. It is chiefly noticed during convalescence; it may lead to suppuration and extensive destruction, and to alarming symptoms of suffocation. In several cases small portions of cartilage have been coughed up, and recovery has taken place; in many tracheotomy is necessary, though this is not infrequently followed by fatal results (81). Some authors (Dietrich, Richle) have looked upon the laryngeal ulcers in enteric fever as allied in their origin and nature to bed-sores, and due partly to pressure and partly to disturbance in the circulation and innervation of the parts; they have accordingly proposed for these ulcers the name of "decubital ulcers."

Lastly, paralysis of the vocal cords has occasionally been observed during convalescence, or some time after. Przedborski found paralysis in 25 out of 100 cases examined. In some cases it has been shown to be due to pressure on the recurrent laryngeal nerve, either by enlarged glands or thickened pleura (Schrötter); in others it is probably the result of changes in the muscles or nerves due to the toxic effect of the poison. Thus in one case paralysis of the vocal cord was associated with multiple peripheral neuritis. (For a more detailed account of the laryngeal affections see 41, 71.)

Bronchitis in some degree is a constant feature of enteric fever; it is characterised by a short cough, with little or no expectoration, and by harsh breathing, with abundant or at other times scanty rhonchi. It may occasionally become very severe, and extend to the smallest bronchi. Bronchopneumonia occurs chiefly in the disseminated form, and may lead to small foci of suppuration. It is commonly due to infection with the pyogenetic cocci; occasionally the typhoid bacillus has been found in the inflamed lung, and the lesion has been regarded as a specific one.

Hypostatic congestion occurs frequently in enteric fever owing to the enforced and prolonged recumbent posture of the patient; it may lead to hypostatic pneumonia or collapse.

Lobar Pneumonia.—Croupous or fibrinous pneumonia is an important complication of typhoid fever. It occurs, according to Dr. Horton Smith, in 5 per cent of the fatal cases. In most cases the pneumococcus of Fränkel is the causal agent, in others a mixed infection has been observed, the pneumococcus being associated with streptococci or staphylococci. In rare instances the pyogenetic cocci alone have been observed, and somewhat more frequently associated with the typhoid bacillus. Some few cases where the typhoid bacillus has been detected in the inflamed lung have been regarded as a primary localisation of the disease (pneumo-typhoid) (96). According to Fränkel (41), however, the occurrence of such a pneumo-typhoid still lacks convincing demonstration. Clinically considered, it must be noted that in some cases pneumonia occurs at the outset of the disease and masks the enteric symptoms for some days, till

in the second week, on the subsidence of the pneumonic symptoms, but slight abatement of the fever follows, and the enteric symptoms become more pronounced; in others, and this is more frequent, pneumonia sets in at the end of the second or third week of the fever. The usual symptoms—such as rigor, pain, and rusty sputum—are often absent, and the affection is often to be recognised only by increased frequency of breathing, by rise of temperature, and by the physical signs; in some few cases, however, acute pleuritic pain and rusty sputum may be noticed. I have seen a case of the combination of septic pneumonia and enteric fever in which the pneumonia was of the creeping kind, attacking first the base and then the apex on each side; the sputum contained masses of streptococci but no pneumococci. During the influenza epidemic the combination of influenzal pneumonia with enteric fever was occasionally noticed (131). The association of pneumonia with true enteric fever must be distinguished from the "typhoid pneumonia," in which diarrhœa and all the symptoms known as the "typhoid" state occur—namely, great prostration, low muttering delirium, etc. In many cases the diagnosis cannot be made until the disease has lasted some days, when its presence is suggested by the marked enlargement of the spleen, the appearance of roseolar spots, the persistence of the fever and the occurrence of intestinal hæmorrhage.

Pleurisy and empyema have occasionally been noticed during the course of enteric. Milder attacks of pleurisy, in which spontaneous absorption of exudation takes place, are not uncommon. Extensive exudations occur much less frequently, and are to be considered as the result of a mixed infection, due to streptococci or pneumococci. The typhoid bacillus in pure culture has also been found in a number of cases, and its etiological significance seems to be beyond doubt (Fränkel, Remlinger).

Pneumothorax is an extremely rare complication; it is invariably a sequel of some gross lesion of the lung. Two cases have been described by Dr. Hale White.

Tuberculosis of the lung has occasionally been observed during convalescence or some time after; probably the disease in these cases was already present in the patient before he caught typhoid. Acute tuberculosis following enteric fever has been noted especially in some of the epidemics of enteric in soldiers during war (54).

The Mouth.—The state of the tongue, as already indicated in the general description, varies with the severity and the stage of the disease. At the onset it is covered with a white fur, which gradually thickens, but is still moist; and in milder cases this condition may not alter throughout the whole of the course; in the ordinary cases after the first week the tongue becomes dry, and is covered by a brown fur; later the dryness still further increases, and the centre of the tongue is covered by a deep brown, almost black, dry fur, which may form crusts and leave fissures. The gums and lips become likewise covered by brown, dry masses of sordes. With the beginning of convalescence the tongue

becomes moist again and quickly cleans. The secretion of saliva is in most cases very much diminished, as indeed is the case in most fevers.

Parotitis is occasionally observed during the later course, most frequently in the third week, or as a sequel, and in very severe cases it gives rise to more or less extensive swelling, and is usually unilateral; the exudation may gradually become absorbed, or suppuration may ensue, which not unfrequently leads to extensive sloughing of the cervical tissues and death. It is more frequently noticed in some epidemics than in others, and is either due to an extension of the inflammation from Steno's duct or to a metastatic inflammation. Schudmak and Vlachos (111) record a case of parotid abscess in which the typhoid bacillus was obtained in pure culture from the pus. Murchison recorded six cases, of which five terminated fatally; Prof. Osler noticed twelve cases, of which four terminated fatally. A remarkable localised sweating in the parotid region is occasionally observed after a suppurative parotitis (Osler).

Cancrum oris occurs chiefly in children, and appears to be much less frequent now than formerly. It is observed during the later stages of enteric, and its commencement, as it begins without pain as a small necrotic patch on the mucous surface of the cheek, is not likely to be noticed. The necrotic patch extends in depth, and soon a hard, brawny, shining, indurated patch, at first pale and gradually deepening in colour, appears on the outside of the cheek; the patch softens, a deep slough forms, and on separation a hole may form through which the gums and teeth can be seen; at the same time the process extends on the mucous surface, causing extensive ulcerations of the gums, and even of the tongue. The gangrene may now spread farther, affecting the greater part of the cheek, the jaw may be laid bare, the teeth become loosened and fall out, and necrosis of the alveoli follow. There is marked salivation, and the breath is very fœtid. In spite of the extensive spreading of the necrosis there is rarely any hæmorrhage, and there is no pain throughout the whole course of the disease. In most cases the patient dies from septic pneumonia or other septic complication. Recovery is very rare, and in this event a marked deformity of the face remains. The affection is of the nature of gangrene, and is not due to typhoid bacilli; long threads of small bacilli have been found in the spreading edge by Dr. Lingard.

Pharynx.—Catarrhal pharyngitis is often observed, and during the latter stage of severe cases there is occasionally a thick deposit on the fauces, which can be detached, and is found to consist of debris, particles of food, masses of epithelial cells, leucocytes, and numerous micro-organisms. In some cases a deposit roughly resembling a diphtheritic membrane is seen; this owes its origin probably to streptococci and staphylococci, which are found in large numbers together with necrotic tissue and fibrin. This is usually a complication of very severe and fatal cases.

A peculiar ulceration has been described by several French and German observers (Bouveret, Devignac, Duguet, Wagner, Cahn), and

is looked upon as specific of enteric fever. It has been named pharyngotyphoid. The ulcers are superficial, circumscribed, cleanly cut, and occur principally on the soft palate, close to the hard palate. From the observations of Rénon it appears, however, that they are not due to typhoid bacilli, but to streptococci and staphylococci.

Œsophagus.—Pain and dysphagia have rarely been met with as a result of ulceration of the œsophagus, and in a few cases œsophageal stricture has followed healing of such ulcers (Osler, Pyle, Dugan, Tinker).

Gastro-intestinal Symptoms.—Nausea and vomiting, as already noticed, may be present at the onset and continue for some days. In most cases these symptoms disappear after the first week, so that the patient, as a rule, has no difficulty in taking large quantities of milk; the secretion of gastric juice is very much diminished, and free hydrochloric acid, as in most febrile affections, is absent. In cases where severe nephritis is noticed during the course of the fever, persistent vomiting, probably uræmic, has been noted. Hæmatemesis is a rare event, except in the hæmorrhagic variety of the disease. Epigastric pain and vomiting, due to inflammatory changes and ulceration of the stomach, have also been recorded (A. Chauffard).

Diarrhœa is one of the characteristic symptoms of enteric fever. It may be present from the first, and persist throughout the whole course, continuing sometimes even when the temperature has reached the normal. Such continuous diarrhœa occurs in about one-third of all cases. In about a similar proportion the diarrhœa is transient or alternates with solid stools. In other cases there is constipation at first, and diarrhœa begins about the end of first week; in others diarrhœa may be absent throughout, and even obstinate constipation may exist. Profuse diarrhœa is noticed principally in severe cases, but there is no relation between the diarrhœa and the ulceration of the intestines, and even in constipated patients extensive ulcerations have been found. The number of stools, usually four to ten in twenty-four hours, varies considerably; sometimes, however, the stools occur even more frequently. With each evacuation a fairly large quantity is discharged. The stool is thin at first, but of the ordinary brown colour; soon it becomes yellowish, of the colour and consistency of pea-soup; it is often uniform, but in children, and sometimes in adults when very large quantities of milk are taken, it contains curds. With the approach of convalescence I have frequently noticed the colour of the stool to become greenish and less uniform, showing small solid particles. The stool, especially in children, has a very foul smell. On standing the stool separates into two layers, a lower, yellowish-grey, flocculent mass and a supernatant, watery, turbid, or translucent fluid, poor in solids (4 per cent), and deficient in albumin and mucus. Microscopically, besides the partly digested particles of food, the stool contains a large quantity of triple phosphates, desquamated epithelial cells, embryonic cells, blood-corpuscles, necrotic tissue-elements, and granular detritus. Numerous micro-organisms are found, micrococci and larger and smaller bacilli. The typhoid bacillus has been found in the alvine

discharges as early as the second day; its detection, especially its distinction from the bacterium coli, which occurs constantly in the fæces both in health and in disease, has already been described; and with the employment of modern methods its isolation affords a valuable means of diagnosis. Careful examination of the stool on the third week often reveals the presence of small shreds, probably sloughs from Peyer's patches. There is usually no pain either before or after the discharge.

Hæmorrhage from the bowels in any marked quantity occurs in from 3 to 7 per cent of the cases (Murchison, Liebermeister). It is much rarer in children, and attains its maximum incidence between the forty-fifth and fifty-fifth years. In some cases it may occur at the end of the first week, and is then probably due to intense congestion; most commonly it occurs after the second week, in Curschmann's experience fully 30 per cent of all intestinal hæmorrhages occur within the first two weeks; it may occur only once, and is then not a very unfavourable symptom, or repeatedly, and there may be eight to ten, and even more discharges in twenty-four hours, consisting of almost pure liquid blood. In two very severe cases (husband and wife) the hæmorrhage was so profuse that pressure on the abdomen, or any movement on the part of the patient, was followed by a discharge of blood, but both patients recovered. In less severe cases the stool is black and tarry. Slight hæmorrhage does not give rise to any subjective symptoms. Profuse hæmorrhage is indicated by a sensation of faintness, rapid fall of temperature (from 2° to 5° F.), pallor of the face, smallness and rapidity of the pulse, and extreme prostration. In some cases Thayer found a leucocytosis reaching its maximum within twenty-four hours. According to Zülzer, whose statement is confirmed by Moore, profuse hæmorrhage, by filling several coils of intestines, may give rise to a dull percussion note where previously the note was tympanitic. Such abundant hæmorrhage during the later stage of typhoid is due either to erosion of the vessels on the separation of a slough, or to an increased diapedesis from the small arteries, whose walls are degenerated (101). As to the prognostic importance of the hæmorrhage authors differ somewhat. Graves, Trousseau, and Griesinger were of opinion that the occurrence of hæmorrhage is not an unfavourable symptom. This is probably correct when hæmorrhage occurs only once and early, as by the hæmorrhage some of the toxic material accumulating in the blood may be got rid of. Profuse hæmorrhage, on the other hand, occurring at a later period, must always be looked upon as a very serious event, though the mortality, from syncope chiefly, varies considerably, from 12 to 40 per cent, apparently as a result of temporary and local influences.

In hæmorrhagic typhoid, with petechial eruption and abundant epistaxis, intestinal hæmorrhage is a prominent symptom, and may occur earlier in the disease.

Tympanites, dependent upon paralysis of the muscular coats of the intestine, is indicative of either severe toxæmia or serious local disturbances, as localised peritonitis or intestinal hæmorrhage. Under

favourable conditions it is generally slight or entirely absent, but when excessive is of grave omen. It may favour perforation, or by displacement of the diaphragm upwards cause cardiac disturbances. Of gurgling and pain on pressure we have already spoken. Abdominal tenderness is sometimes observed for the first week or later; it is sometimes diffuse, at other times limited to the region of the umbilicus, or the right iliac region. Persistent and localised pain is probably due to slight peritonitis. M'Crae (83) in 500 cases of typhoid fever at the Johns Hopkins Hospital found that about two-fifths were free from abdominal pain or tenderness, and that rather less that one-fifth had tenderness only. Pain due to conditions other than the specific intestinal lesions was present in about 14 per cent of the cases. It occurred with hæmorrhage or perforation in about 5 per cent of all cases. It was most constantly present with perforation. In about two-fifths of all cases with pain no cause could be found.

Perforation of an intestinal ulcer is one of the most terrible of accidents. It seems to occur in about 2·5 to 3 per cent of all cases of typhoid, whilst amongst fatal cases its incidence varies in different statistics from 4 to 30 per cent, the more usual percentage being from 9 to 12. It is rarer in children, and occurs more frequently in men than in women. It may occur any time after the second week, and it has been observed after all fever symptoms have subsided, as late as the sixtieth and hundredth day of the disease. Prof. Osler observed one case as early as the eighth day. In Hoelscher's table, of the 114 fatal cases, no case is recorded in the first two weeks of the fever (59). As accessory causes, indigestible food, excessive tympanites, obstinate vomiting, movements on the part of the patient, and the presence of intestinal worms are cited; but occasionally perforation may occur without any such aids. It may occur in mild cases, and I have noticed it in apyrexial typhoid. Statistics from the Johns Hopkins Hospital show that it is more likely to occur in cases with diarrhœa. Perforation occurs most commonly in the lower portions of the ileum near its cæcal end; the cæcum, the parts adjacent to the ileo-cæcal valve, and the appendix are also not infrequently the seat of rupture. Perforation of the colon in any of its parts may occur, but the ascending and transverse portions are the favourite seats. In the jejunum perforation is very uncommon. The perforation is generally single, occasionally two or three openings close together are found, rarely are they widely separated or more numerous. The size and character of the perforation vary with its mode of origin; in cases where it results from the direct involvement of the peritoneum in the necrotic process, the opening is large and oval in form; where it results from a slow, progressive ulceration there are several small cribriform openings; whilst mechanical rupture of the attenuated base of an ulcer is distinguished by the longitudinal, slit-like, ragged character of the openings. The perforation, setting in suddenly, quickly gives rise to the symptoms of perforative peritonitis: severe pain, at first situated over the right iliac fossa (or referred pain over the left iliac region), soon

becomes general. The pain may be persistent, or more like colic; in some few cases it has been entirely absent. Vomiting usually occurs early; the patient shows symptoms of collapse; the features become pale and pinched, the pulse small and thread-like. Following perforation there is in many cases a rapid relative increase in the number of leucocytes. The abdomen generally becomes more distended, and the liver dulness can no longer be made out on percussion (Wagner, Flint); in some cases the abdomen, instead of being distended, may be retracted, with marked rigidity of the walls (Wagner). The breathing becomes thoracic, and the temperature suddenly falls, though it may afterwards rise again considerably. There is often suppression of urine. Soon the prostration becomes extreme, the voice husky, cold clammy perspiration covers the face and body, and the patient gradually sinks, the sensorium often remaining clear to the end. In some cases death may occur at a later period from subacute peritonitis. Thus a patient was admitted into the Manchester Infirmary with symptoms of intestinal obstruction which had lasted for some days; the patient died soon after admission. At the autopsy typical typhoid ulcers were found, one of which was perforated, and fæcal extravasation had taken place. There was extensive peritonitis and a small quantity of fæcal matter lay free in the abdomen. Recovery does occasionally, but very rarely, occur. If the perforation be a tiny one the symptoms may not be very characteristic; the pulse, however, will rise over 120, and the temperature may fall. The area of liver dulness may also be diminished, and the respiration be thoracic. There may be a disposition to vomit, and a little increasing pain.

Perforative peritonitis, apart from the perforation of an ulcer, may occur from gangrene of the bowel, ulceration of the gall-bladder, rupture of a suppurating mesenteric gland, or of abscess of the liver or of the spleen, rupture of spleen, etc.

Peritonitis without perforation may result from extension of the inflammation to the serous coat of the intestine, or it may be possibly of hæmatogenous origin. It is then generally circumscribed, and tends to form adhesions. Occasionally it may give rise to local suppuration.

In the treatment of perforative peritonitis, operative interference undertaken early offers the best prospects. In 255 cases of laparotomy for this complication collated by Zesus, recovery occurred in 95. Out of 67 operated on within twenty-four hours of perforation 30 recovered, while out of 23 in which operation was further delayed 3 only recovered.

Liver and Biliary Passages.—In the more severe forms of typhoid infection the liver is frequently found to be the seat of early parenchymatous inflammation, which is occasionally manifest during the height of the disease by some enlargement and tenderness of that organ. The scattered focal lesions which are a frequent post-mortem phenomenon have apparently no clinical significance. More severe forms of parenchymatous hepatitis are rarely met with, but acute yellow atrophy has been recorded as such a sequel.

Jaundice is very rare in the enteric fever of our climate, though its

frequency seems to vary in different epidemics; in hot climates and also where there is an associated malarial infection it is a much more frequent complication. It may be a manifestation of catarrhal cholangitis, cholecystitis, gall-stones, hepatic abscess, acute yellow atrophy, or it may be of toxic origin.

There is some diversity of opinion as to the nature of the slighter forms of jaundice occurring in cases of moderate severity. Prof. Osler regards the majority as depending upon obstructive catarrhal inflammation of the bile-ducts caused by the typhoid bacillus, which is almost constantly present in the bile. Da Costa, on the other hand, on the basis of the late occurrence of the jaundice, of its greater frequency in severe cases, and of the presence of bile in the fæces, regarded such jaundice as toxic in origin.

The typhoid bacillus has been found almost constantly in the gall-bladder (Chiari, Birch-Hirschfeld, and others), often in enormous numbers, frequently clumped, and virulent. In most cases, however, the gall-bladder and ducts are normal, and accordingly some other factor must contribute to the various lesions of these structures which are ascribed to the typhoid bacillus. The relation of gall-stones to the presence of the bacillus in the gall-bladder is of interest. It has long been recognised that gall-stones are a not uncommon sequel of typhoid fever. In many cases the typhoid bacillus has been isolated from the interior of calculi. Gall-stones have been produced experimentally by the inoculation of typhoid bacilli into the gall-bladder of animals, and it is believed that the clumps of bacilli in the bile may form the nuclei for the formation of calculi (Gilbert and Fournier, Richardson).

Hepatic abscess in association with typhoid fever is represented in 22 cases collected by Da Costa. Of these only 7 had jaundice. The lesion, which apparently is never caused by the typhoid bacillus, may arise as a manifestation of a general pyæmia, or of a portal pyæmia—suppurative pylephlebitis—consecutive to suppurative lesions in the intestinal tract, or, lastly, as a result of extension from various suppurative lesions of the gall-bladder and large bile-ducts.

Acute cholecystitis has been met with a considerable number of times during the febrile attack, and in many pure cultures of the typhoid bacillus have been isolated from the inflamed viscus. Rupture of the inflamed gall-bladder into the peritoneum, and extension of the inflammation to the liver with the production of hepatic abscess, have been occasionally recorded.

Spleen.—The enlargement of the spleen is a constant feature in enteric fever, and its gradual increase can often be demonstrated during the course of the disease. During the second week, especially in children, the edge of the spleen can often be readily felt, particularly on deep inspiration. The enlargement continues to the end of the third week, when it gradually subsides. The spleen is found increased in its various dimensions, and the enlargement can be readily made out by percussion. When there is great distension of the abdomen, or when

the stomach or colon are inflated and displaced, the splenic enlargement cannot easily be made out; in other cases the area of splenic dulness, though not enlarged, is increased in intensity. Palpation of the spleen is occasionally painful. Abscesses and rupture of the spleen have been occasionally noticed; they are, however, extremely rare, and more of pathological than clinical interest.

Genito-urinary System.—The urine in enteric fever presents the ordinary characters of febrile urine. It is decreased in quantity, especially during the first three weeks of the disease; with convalescence the quantity increases, and not infrequently there is a marked polyuria, as much as 10,000 c.c. or more being excreted in the twenty-four hours. The urine is then almost colourless and of very low specific gravity, 1002. In rare instances polyuria is noted throughout the entire course of the disease, the quantity only falling to normal with convalescence (Fussell, Carmany, and Hudson). With the reduction in quantity during the febrile stage, the urine is high-coloured, very acid, and of high specific gravity. Uric acid, kreatinin, and ammonia are increased; urea is almost invariably and markedly increased, though sometimes it is diminished during the first few days. The chlorides are always considerably diminished during the febrile stage. Terray, in comparing the quantity of sodium chloride in the food with that voided in the urine and the fæces in four cases of enteric fever, found the chlorides diminished during the whole febrile period, and also for some days after the fever had disappeared. The diminution, according to Leyden, is due to the retention of water in the system during the fever. Phosphoric acid (Zuelzer) is also diminished, the potash salts and conjugated sulphuric acid (Zuelzer) increased. Of abnormal constituents, albumin is found in 70 to 80 per cent of the more severe cases (74 per cent Osler, 15 to 20 per cent Curschmann). Of the various forms of albumin, serum-albumin is constantly found, serum-globulin often, hemi-albumose or propeptone occasionally. In several cases the urine has given the reactions of hemi-albumose for one or two days, which has then been replaced by serum-albumin. The urine may contain blood when hæmorrhagic nephritis complicates enteric fever, and in hæmorrhagic typhoid. In some severe cases hæmoglobinuria has been observed. Urobilin may be present in considerable quantity; a condition which Sessier and others associate with changes in the liver. Indicanuria is also a frequent condition. Mucus occurs when cystitis is present. In some cases acetone and aceto-acetic acid are found in the urine without the presence of sugar. Bernert noted acetonuria in eleven out of ninety-four cases examined; he believes it orginates from inanition. Alimentary glycosuria was found by Maximow in a large majority of cases during the febrile period and during convalescence; its occurrence appeared to be particularly favoured by the incidence of pulmonary complications. Microscopic examination may reveal the presence of various forms of casts, as will be presently pointed out. In very severe cases leucin and tyrosin have been found.

Ehrlich's Diazo-Reaction.—Ehrlich described this test in 1882, and

since then a large number of observations have appeared on the subject (56). The peculiar reaction is probably due to the presence of some nitrogenous products in the urine. To carry out the test two solutions are used: No. 1, a saturated solution of sulphanilic acid in dilute hydrochloric acid (1 in 20); No. 2, a solution of sodium nitrite in water (0·5 per cent). The urine to be tested is put into a test-tube, and a quantity of the solutions 1 and 2 equal to that of the urine is added (about 40 c.c. of the sulphanilic acid and 1 c.c. of sodium nitrite solution), the mixture is well shaken, and then some drops of liquor ammoniæ are allowed to run down the side of the tube. At the junction of the two a deep brownish-red ring appears; if again shaken the whole fluid-mass appears red, and if the diazo-reaction be present the foam also appears rose-tinted. This test has undoubtedly some diagnostic and prognostic value (124). It is present in a very large majority of cases of enteric fever both in adults and in children, and even in the apyrexial type; it appears early, often before the serum-reaction (Hewetson noticed it in 77 per cent of his cases in the first week), and it often disappears during the third and fourth week, and in severe cases this disappearance is coincident with improvement in the condition of the patient. In relapses, if the reaction has already disappeared, it generally returns, whilst in other forms of post-typhoid pyrexia it remains absent. The reaction, however, is also seen in other febrile affections (typhus, measles, scarlet fever, pneumonia, acute tuberculosis), and in some apyrexial diseases (chronic hepatitis, carcinoma, leukæmia, etc.), and its diagnostic value is accordingly rather of a negative character, in that the continued absence of the reaction is strongly (50 to 1) against the diagnosis of typhoid.

Albuminuria is an important symptom; it is not always due to the same cause, and from analogy with other infectious diseases, and from a consideration of the pathological changes in the kidney found after death, we may distinguish the following forms:—

1. Febrile Albuminuria. — The albuminuria is here due to the pyrexia,[1] though the retention of toxic products in the blood cannot be neglected as a probable cause. Clinically this albuminuria is characterised by the small amount of albumin in the urine without blood, and often without casts; if casts be present they are hyaline and few in number. This albuminuria may be noted early, sometimes even in the first week, though it is most frequently observed during the second week. It occurs in children as well as in adults; it is sometimes absent for a day or two, and, as a rule, it disappears with convalescence; occasionally it persists throughout convalescence and even for long periods after. It is not associated with any very serious symptoms, and is not followed by any permanent damage of the kidney; yet, as Curschmann points out, the

[1] As it has been demonstrated by means of Roy's oncometer that with an increase of the body-temperature the kidneys decrease in size considerably, the diminished quantity of urine passed and the presence of albumin in the urine are readily explained (86); again, experimental investigations have shown that albumin may appear in the urine of animals exposed to high temperatures.

mortality among cases showing febrile albuminuria is abnormally high, 27·2 per cent.

2. Albuminuria due to Acute Bright's Disease (Hæmorrhagic Nephritis, Nephro-typhoid).—The albumin is here often abundant; the urine contains blood, and granular, fatty, and blood casts are seen. Various micro-organisms, amongst them the typhoid bacillus, have been found occasionally in the urine during life, or in the kidneys after death in this affection. This complication, if stress be laid on the free admixture of blood, is of rare occurrence—the presence of large quantities of albumin and casts without any blood, or with but a small quantity of blood, is of more frequent occurrence (Osler's figures give about 10 per cent of the observed cases of enteric fever). This complication is usually observed in the second week, but sometimes (Gubler, Robin) it may be an early symptom. It may last for several days, generally from one to two weeks, and end in recovery; or uræmic symptoms, low delirium, and convulsions may set in. When this complication occurs early with pain in the back and the passage of urine containing much blood, and is followed by uræmic symptoms, the primary disease is difficult to recognise. In none of these cases has the condition progressed to a chronic nephritis. The affection is most likely due to the action of bacterial products on the kidney, products which either circulate in the blood or pass to the kidney from another part of the urinary tract (90): thus it is allied to the nephritis seen in other infectious fevers, and scarcely deserves the designation of nephro-typhoid.

3. Acute Suppurative Nephritis is an occasional complication of enteric fever; in most cases it results from secondary septic infection, but may be due to the action of the typhoid bacillus, as in a case recorded by Flexner. The lymphomatous nephritis described by Wagner is probably an early phase of this condition. There are no diagnostic symptoms, except perhaps the presence of polymorphonuclear leucocytes in the urine not due to any other complications in the urinary tract, such as cystitis.

4. During convalescence albuminuria may be observed with other symptoms of nephritis, and be followed by œdema. It is allied to the post-febrile nephritis seen in other infectious fevers (Osler).

Typhoid Bacilluria.—Typhoid bacilli are found in the urine in about one-third of all cases, and then may be in such abundance as to give to the urine a characteristic shimmering turbidity. They first make their appearance in the later stages of the disease, about the fifteenth day, and may persist for variable periods, months or years, after convalescence (seven years in a case reported by Young). They are almost always associated with the presence of albumin and casts in the urine, and frequently with a variable degree of pyuria. Dr. Horton-Smith explains the occurrence of bacilluria by the excretion of stray typhoid bacilli through the kidneys and their immediate multiplication in the bladder urine.

Cystitis is always accompanied by bacilluria and varies much in

severity. It would appear that the presence of bacilluria in itself is not sufficient to cause typhoidal cystitis, but retention or damage to the bladder-walls are essential factors. Some cases run a very protracted course. Brown records an example which shows that the bladder may be infected by the introduction of the typhoid bacillus on a sound or catheter.

Genital Organs.—In the male *orchitis* and *epididymitis* occur in young subjects and during convalescence; the right side is more usually affected. The patient again becomes feverish, the testicle is very painful and swells rapidly. Resolution sets in quickly, or rarely suppuration ensues. Exceptionally the condition terminates in atrophy of the testicle.

In the female, *ovaritis* and *salpingitis* have also been noticed occasionally. Amenorrhœa or slight irregular hæmorrhage is the rule during the entire febrile period and the early days of convalescence. In hæmorrhagic typhoid there may be profuse metrorrhagia; acute bartholinitis, gangrene of the vulva, leucorrhœa, and mastitis are rare complications. As regards pregnancy, the collected statistics of Sacquin show that out of 223 cases of pregnancy during typhoid, abortion or premature labour occurred in 150, with a mortality of 16 per cent.

Symptoms relating to the Nervous System.—The nervous system is often profoundly implicated in enteric fever throughout the febrile period and even after; so much so that in Germany the popular designation of typhoid is nervous fever (*Nervenfieber*). The nervous symptoms vary considerably in individual cases.

At the onset, and sometimes even during the incubation-period, headache and insomnia are the principal features; these usually subside after the first week. True neuralgia, especially of the supraorbital, infraorbital, and occipital nerves, is occasionally a feature of the onset. In milder cases there may be no other nervous symptoms; in the more severe cases there are symptoms of irritation, and in the most severe cases evidence of paralysis of the higher centres. Some of these have already been alluded to in the general description of the disease.

Delirium is common in the ordinary, and especially in the severer cases. In the milder cases it may only occur at night, when the patient awakes from a light slumber; in the more severe cases it is persistent, but varies in its manifestations. There may be quiet delirium in which the patient is easily roused, answers questions fairly rationally, but soon lapses into delirium again: violent delirium, when the patient gets very excited, talks or sings, or may even become violent; this may lead gradually to acute maniacal delirium, sometimes occurring in paroxysms, during which the patient must be carefully watched, as he may attempt to escape or do himself some bodily injury. It must be remembered that even without showing marked signs of delirium patients in enteric fever may manifest suicidal tendencies. Low muttering delirium is seen in the more severe cases: the patient is restless, mutters constantly, and trembles and twitches; equally serious is the delirium in which the patient is quiet, lies with his eyes open, but is quite uncon-

scious. The more severe forms often lead to coma. In tipplers the delirium often takes the form of delirium tremens—the patient converses with imaginary people, fancies himself at his usual avocations, gives orders, or serves customers, and so forth.

In some cases, especially in women, the delirium has more the character of lipemania; the patient imagines herself the subject of some persecution, she refuses to speak, keeps herself wrapped up in the blankets, appears terrified when any one approaches, and is often absorbed in one fixed idea (4). The fixed idea from which the fever patient suffers sometimes persists for a while during convalescence. In one case a patient fancied he had received a commission in Her late Majesty's service, and after he had recovered from the fever searched over all the newspapers to see if he had not been gazetted.

In most cases the delirium occurs during or after the second week, but occasionally it is an early symptom, and when preceded by headache, and accompanied, as it sometimes is, by retraction of the head and neck, convulsions, tâches cérébrales, etc.,—and these occur more particularly in children,—the diagnosis from meningitis is often difficult.

The muscles often show increased irritability, and when marked emaciation is present they exhibit idiopathic contractions on being tapped. Muscular tremors affecting the limbs (the upper extremity more than the lower extremity), the tongue, and sometimes the muscles of the face, often accompany other severe nervous symptoms; and subsultus tendinum in enteric as well as in other affections is a grave though not a fatal omen.

Convulsions are noticed sometimes in children, both at the onset and during the course of the disease; in adults they occur sometimes in the meningeal form, or from uræmia in the so-called nephro-typhoid; or they may precede death when myocarditis complicates enteric fever. Severe nervous symptoms are seen, especially in those patients who have a marked neurotic disposition, either acquired or inherited; though the effects of the typhoid toxin cannot be excluded.

Meninges.—Symptoms of meningeal irritation may mark the onset of the disease (meningo-typhoid), or they may occur during the febrile period. They are more frequent in young subjects and in females; in relative frequency they vary in different epidemics. They consist in severe persistent headache, vertigo, tinnitus, photophobia, tâches cérébrales, later pains in the sacral and cervical regions with painful rigidity of the spine and retraction of the head. In addition there are twitchings, perhaps convulsions, pains in the extremities, and tenderness of the skin and muscles. The reflexes, superficial and deep, are increased. Polyuria may be noted, and facial herpes occurs with striking frequency. These manifestations may last from 4 to 12 days or more; they bear no apparent relation to the severity of the other symptoms of the disease, and they may be the cause of death. The onset may be marked by one or a succession of rigors and the appearance of herpes. In fatal cases where the meningeal symptoms have been slight and not the cause of

death, there are but slight gross indications of any lesion; microscopically, however, Schultze in such cases has demonstrated the existence of a perivascular small-cell infiltration in the pia-arachnoid and also in the substance of the cortex. The more severe and fatal cases usually present all the features of an acute purulent cerebrospinal meningitis, of which the causal agent has been determined in a number of cases. In some the typhoid bacillus has been isolated in pure culture; in others, particularly when associated with pulmonary complications, the pneumococcus has been found; in a few the meningococcus, and again in others the ordinary pyogenetic cocci.

Brain.—Hemiplegia, with facial and hypoglossal paralysis, and aphasia may occur as a consequence of hæmorrhage, thrombosis, embolism, or abscess; the condition is generally met with in the febrile period or during convalescence. In 17 cases of typhoidal hemiplegia collected by Dr. F. H. Hawkins, aphasia was present in 12. A curious form of aphasia is occasionally seen in young subjects during convalescence, in which the disturbances of speech occur alone or are accompanied by only circumscribed paralysis; motor disturbances in the trunk or the extremities if present at all are of the nature of tremor or ataxia. This condition is generally recovered from rapidly. Occasional examples of cerebral monoplegia recorded in the literature may be varieties of peripheral neuritis.

Lesions, hæmorrhage and softening, of the medulla as complications of typhoid fever are recorded by Kummell, Eisenlohr, and Curschmann. In the three cases described by Eisenlohr, the patients were attacked during the febrile stage with symptoms of bulbar paralysis affecting the lips and tongue, interfering with articulation and accompanied by weakness in the muscles of the trunk. One of the cases terminated fatally, and a staphylococcus and a peculiar bacillus were found in the medulla, cord, and brain.

Spinal Cord.—Among affections of the spinal cord noted in association with typhoid fever, a number of cases of myelitis with symptoms of acute ascending paralysis have been recorded by Leudet, Curschmann, Raymond, Ganioz, and others. The condition has occurred during the febrile period (second week) and during convalescence, from the third to the seventh day of apyrexia. According to Ganioz the onset is abrupt without prodroma; the legs are first affected, the paralysis involving in ascending order the muscles of the toes and foot, then of the thigh and pelvis, then of the hand and arm, the trunk, the muscles of respiration, the tongue, the pharynx, and œsophagus. The sphincters may or may not be involved. There are neither sensory troubles nor muscular atrophy. The reflexes are usually abolished. Towards the end, bulbar symptoms appear. The paralysis may be complete in from one to seven days, and is invariably fatal. Ganioz regards such cases as due to the action of the typhoid toxin on the nerve-elements. In Curschmann's case, typhoid bacilli were demonstrated in the spinal cord. A curious case of acute hæmorrhagic transverse myelitis is recorded by Schiff in a patient aged nineteen

years, which proved fatal in eighteen hours. On the ninth day of the disease complete motor and sensory paralysis below the fourth cervical segment, with absent reflexes, appeared suddenly without prodroma. The autopsy revealed a hæmorrhagic myelitis confined to the fourth and fifth cervical segments. Typhoid bacilli could not be found in the lesion nor in the cerebrospinal fluid.

Westphal has noticed a peculiar form of ataxia associated with tremor in the lower extremities, and disorders of speech of the bulbar type following typhoid fever.

Disseminated sclerosis is more frequently a sequel of typhoid than of any other infectious fever. In 25 cases following infectious disease, collected by Marie, 11 followed typhoid.

The reflexes are not uncommonly affected apart from gross nervous lesions in typhoid. In 100 cases examined by Remlinger the knee-jerks were abolished in 29, diminished in 22, and exaggerated in 32. It would seem that exaggeration of the reflexes is of serious prognostic omen.

Peripheral Nerves are more frequently involved than the spinal cord. The lesion—a neuritis—may give rise to a localised atrophic paralysis, to a paraplegia, or it may be in the form of a pronounced multiple neuritis. It generally occurs towards the end of the febrile period or during convalescence. The localised forms appear to affect the lower extremities most frequently. Of the multiple neuritis, Ganioz remarks that the onset is insidious; the sensory symptoms appear first as paræsthesia or active pain, giving place later to anæsthesia, with pain on pressure over the nerves or muscles. Ordinarily, the motor paralysis is not complete, and the reflexes, generally diminished or absent, may occasionally be increased. The reaction of degeneration may be present, but it is apparently not so frequent in this as in other forms of multiple neuritis.

Paralysis of cranial nerves is very rare in enteric fever. I have seen one case in which the root (both sensory and motor) of the fifth was evidently affected; partial recovery took place. Occasionally paralysis of one or other of the ocular muscles has been noticed. One such case I saw in a young girl (106), and the other in a child three years old, in whom contraction of both hands and feet set in after the paralysis had been established, but it yielded completely to treatment.

It has been pointed out by Dr. Greenhalgh that a cutaneous area (reflex zone) representing the distribution of the last seven dorsal nerves, which through the nervous system is in direct association with the inflamed intestine, presents phenomena indicative of marked depression or inhibition of the functions of the superficial nerves. Of the superficial reflexes he found the abdominal reflex diminished or absent in 77·7 per cent; the epigastric reflex was similarly affected in a like percentage of the cases he examined. The filomotor reflex was absent in all cases. There was also appreciable diminution of tactile sensibility and of the vaso-constrictor impulses in this zone. Evidence of the loss

of vaso-constrictor impulses is seen in the facility with which the tâche cérébrale can be elicited in this belt of skin after the first week of the disease. To this phenomenon Dr. Greenhalgh is disposed to attach some diagnostic importance.

Neurasthenia in its various forms may supervene—cerebrospinal, spinal, sympathetic, and visceral. Under the name of "typhoid spine," cases of spinal neurasthenia, characterised by severe pain in the back and sometimes in the legs, have been described (90).

Local pain, allied to local neurasthenia (topalgia of Blocqui), is occasionally noticed. The affection described as tender toes (acroparæsthesia of Schulze), that is, an excessive tenderness on the slightest pressure of the toes, sole of the foot, and sometimes dorsal surface of the foot, also belongs to this group ; the opposite of this, more or less persistent anæsthesia of a circumscribed area, not due to peripheral neuritis, is occasionally seen. Local vasomotor neurosis, consisting of redness with slight swelling of parts of the extremities, has been described.

Mental Diseases.—Loss of memory and feebleness of intelligence, leading to dementia, melancholia, monomania, and other forms of insanity may appear. Some of these symptoms, probably due to malnutrition, are of short duration ; others, probably due to the toxic effect on the nerve-elements, are of longer duration ; in some cases recovery takes place after many months, whilst others remain incurable.

Hysterical manifestations during convalescence are not frequent, yet are occasionally seen both in men and women.

Ear.—Apart from temporary deafness, met with almost characteristically at the height of the fever, hearing may be affected in enteric fever [in 4 per cent (Bezold)]. In many cases the deafness is due to otitis media, which in the course of time may be followed by the well-known cerebral complications—meningitis, thrombosis of cerebral sinuses, abscess of the brain. Sometimes the deafness is due to an affection of the auditory nerve, and is more permanent.

Eye.—Optic neuritis is a rare complication. It is usually associated with meningitis, but may occur apart from any intracranial complication. I have seen one case in which amblyopia and colour-blindness occurred in one eye after the fever, and the optic disc was blurred ; this probably was a case of retrobulbar neuritis. According to Bull, retinal hæmorrhages are not uncommon during the height of the disease. Ulceration of the cornea and suppuration of the orbit have been described (Panas).

Bone and Joint Affections.—The typhoid bacillus has been found in the bone-marrow during the disease, and as long as four months after convalescence (Quincke), and it is therefore not astonishing to find that affections of the bones are not uncommon sequels of enteric fever. The most common event is the formation of an abscess, periosteal or myelogenic. The tibia, ribs, and femur are the usual seats of these abscesses, though they may occur in other bones. In the pus streptococci or staphylococci have been found ; in some, however, only the typhoid bacillus. These abscesses, ushered in by severe and persistent pains,

redness, and swelling of the affected part, may appear during the febrile period, more commonly from one to three months after the fever, and sometimes much later; in a case recorded by Buschke, seven years had elapsed since the occurrence of enteric fever, yet the typhoid bacillus found in the pus was capable of cultivation. In other cases the bone, instead of undergoing suppuration, becomes hypertrophic and deformed —hypertrophic osteitis.

In children and young persons, after convalescence one occasionally notices an exaggerated growth of the bones. Sometimes a circumscribed periostitis is recorded, which comes on without any great pain, and may undergo complete absorption (Hutinel).

The joint affections associated with or following enteric fever vary in their nature.

1. *Typhoid Arthritis.*—A specific arthritis may occur during convalescence, either in a monarticular or polyarticular form. Of these the monarticular form, involving the hip, is the most frequent and serious; of other joints, the elbow, shoulder, ankle, and knee may be involved. Spontaneous dislocation of the hip is very liable to occur. The polyarticular variety affects the joints of the lower extremity somewhat more frequently than those of the upper.

2. Septic arthritis, usually with other pyæmic symptoms, is seen in mixed infections.

3. Occasionally rheumatic arthritis, affecting one or several joints, may complicate and follow enteric fever, and be accompanied by endocarditis (132).

Typhoid Spondylitis.—Under this term Quincke, Gibney, and others have described a painful stiffness in the lumbar spine, with some local swelling and tenderness coming on during convalescence. In some cases there are manifestations of pressure on the cauda equina, paresis of the legs, exaggerated knee-jerks, and sensory disturbances. It is apparently a serous inflammation of the periosteum and adjacent structures (perispondylitis). A painful condition of the spine (typhoid spine) is also met with from other causes, as muscular strain, possibly with some interstitial myositis, and as a manifestation of neurasthenia.

Thyroid Gland.—Inflammation of the thyroid (typhoid thyroiditis) has been noted in a number of cases; it is almost always unilateral, giving rise to painful enlargement, and rarely dyspnœa. It may terminate either in resolution or suppuration. In the latter the typhoid bacillus, either alone or along with pyogenetic cocci, has been isolated from the pus.

The Nutrition of the Body in Enteric Fever.—Emaciation is most pronounced, especially during the latter part of the attack. According to Robin (105), a person suffering from enteric fever eliminates more solids (52 grammes) than a healthy, well-nourished person (50 grammes). This, apart from many other factors, would explain the emaciation. The daily loss of weight is about 238 grammes. Klemperer's observations further show that during the fever the albumin in food is not completely

used up by the patient, who therefore gives up part of his body-albumin. Ziemec found an average daily loss of body-weight of 0·9 per cent during the fever, a figure much lower than Robin's.

Relapse.—I have already spoken of a recrudescence of the pyrexia during convalescence from various causes. From this the true relapse must be distinguished, which is indeed a fresh attack of enteric fever, and in it appear many of the noteworthy symptoms, such as tympanites, diarrhœa often with slight hæmorrhages, a second series of roseolar spots, a further enlargement of the spleen, and pyrexia with marked evening exacerbations. These symptoms, of course, are not all constantly present. In the presence of the eruption, the diazo-reaction, and the renewed pyrexia, and in the absence of any local inflammation, the diagnosis of a true relapse must be based.

Authors differ somewhat as to the frequency of relapse. Murchison's estimate is 3 per cent, Griesinger 6 per cent, Shattuck 16 per cent, whilst Curschmann gives from 6 to 12 per cent. Men appear more liable to it than women. The duration of the relapse varies from nine to twenty-one days; thus it is shorter, and as a rule the symptoms are less severe than in the primary attack. In Shattuck's twenty-one cases of relapse there was only one death.

The relapse may occur early or late during convalescence; in several cases I have seen it occur only a few days after defervescence; in most cases it occurs within the first fortnight of convalescence, whilst occasionally even a month or more may elapse before its occurrence.

The first relapse may be followed by a second, and sometimes even by a third and fourth relapse, but as a rule the subsequent attacks are shorter in duration and milder in their symptoms. The cause of the relapse is most likely a reinfection from some bacillary nidus which had remained latent—the infection of healthy lymphoid elements by sloughs thrown off from those first affected, by bacilli from the gall-bladder, or by the colonisation of bacilli in the spleen (Rafferty).

Varieties of Enteric Fever.—The diversity in the symptoms and course of enteric fever has led authors to distinguish certain varieties of enteric fever. The usual classification, one which recommends itself from a clinical and practical point of view, is the following:—

1. The Abortive Form.—The disease begins, like an ordinary attack of enteric fever, with high temperature, repeated shivers, enlargement of the spleen, diarrhœa, and roseola, or some of these. Early in the second week the fever falls, and by the end of the week there may be complete defervescence. Relapses have been noticed.

2. The Mild Form.—The symptoms are slight throughout the course of the disease, which lasts from sixteen to twenty-one days; the temperature does not reach 103° F.; diarrhœa, if present, is mild; the prostration not great. There is no great emaciation, and convalescence is usually rapid.

3. Ambulatory Typhoid (walking typhoid, or latent typhoid).—The symptoms are here so slight that the patient follows his work, though

more or less troubled with loss of appetite, diarrhœa, and headache. Patients suffering from this form have often been known to walk to the out-patient room, where, by the condition of the tongue, the tremor, and the temperature, the true nature of the case is recognised. In other cases violent delirium or profuse intestinal hæmorrhage is the first symptom which brings the patient under the doctor; and if death occur soon after, as it often does, extensive intestinal ulcerations are found; or sudden death may occur from perforation (130). I remember a workman who, whilst repairing the roof of a house, fell off and was killed by the fall; at the post-mortem examination, besides fracture of the skull, there were found typical typhoid ulcers in the ileum. At the inquest the wife of the deceased stated that her husband had complained of headache, lassitude, and giddiness for some days.

4. The Apyrexial Form, which runs its course without any perceptible pyrexia.

5. The Grave Form of enteric fever, characterised by high fever and grave nervous symptoms. According to the more prominent symptoms we distinguish under this head—(*a*) The Bilious Form (fièvre bilieuse).—Frequent and persistent vomiting of bilious matter, with severe and persistent headache; pulse quick and small; the case often ends fatally about the end of the second week from asthenia; delirium is generally absent. (*b*) The Ataxic Form.—Delirium with hallucinations prominent, typhoid symptoms severe, and sometimes convulsions. (*c*) The Adynamic Form.—From the outset there are great prostration, very weak heart's action, abundant diarrhœa, low delirium, profound stupor: if these symptoms are associated with subcutaneous and internal hæmorrhages the case is spoken of as the hæmorrhagic form.

Hæmorrhagic Typhoid (fièvre hémorrhagique putride).—This grave form is exceedingly uncommon. Four examples occurred among 6513 cases of typhoid (Uskow). The symptoms are those of severe typhoid associated with hæmorrhage in the skin, mucous membranes, serous cavities, and in the substance of various organs. Hæmorrhages may occur from the onset, or they may only appear with the incidence of a secondary infection (bacillus coli, staphylococcus pyogenes aureus), or they may be a cachectic manifestation or the expression of some idiosyncrasy. Gerhardt believed this form to have become more frequent since the introduction of the cold bath. The condition may end in recovery.

Most of these severe forms are due to a secondary infection of septic nature. Pharyngo-typhoid, laryngo-typhoid, pneumo-typhoid, nephro-typhoid, cardio-typhoid are often instances of mixed infection, as already mentioned.

6. Spleno-typhoid occupies a somewhat different position. It is characterised clinically by a type of fever which in the excessive enlargement of the spleen, and in the absence of intestinal symptoms, rather resembles that of relapsing fever (though spirochætes are not found in the blood). The lesions in Peyer's patches are not well developed, only

congestion and swelling being noticed (33). Sir J. Moore (87) observed a case in which Peyer's patches were not even hyperæmic.

7. Enteric fever in children is not rare. Some of the peculiarities observed in infantile enteric fever have already been noticed. In some cases the infection runs the same course as in the adult, in others the fever has a remittent type (infantile remittent fever), the evening temperature being 2° to 3° F. higher than the morning temperature. Abortive enteric fever is also noticed, likewise the bilious form. A respiratory or thoracic type has been described by some, the more prominent symptoms being quickened respiration, marked dyspnœa and cyanosis, and the presence of fine rales over one or both lungs. A meningeal type may be distinguished which sets in with headache, vomiting, and convulsions, and is followed by delirium, great prostration, and torpor. Diarrhœa and involuntary discharge of fæces is not infrequent, and the diagnosis from meningitis is often difficult. In these cases strabismus, inequality of pupils, injection of the conjunctivæ, and even the hydrocephalic cry (9), may occur. Finally, a spinal type, with hyperæsthesia of the skin, contraction of muscles and opisthotonos (38), is also described.

8. Enteric Fever in the Aged.—Enteric fever is not common in persons after forty; but in epidemics old people are not infrequently affected. I have seen a typical case of typhoid in a man seventy-five years old.[1] The affection usually commences insidiously with headache, loss of appetite, epistaxis; the fever is not very high, and rarely reaches 103°; diarrhœa is present, but not usually profuse. Death sometimes takes place before the end of the third week from pulmonary œdema or failure of the heart. The mortality is high.

9. Malario-typhoid.—See articles on Malaria and Fevers of the Tropics.

10. An epidemic atypical form of enteric fever, occurring only in those who shortly before had suffered from malaria, is described by Karlinski (63). It was observed in Bosnia, and called there dog-typhoid (*Hunde-typhus*). (The typhoid bacillus was found in the fæces in these cases.)

Diagnosis.—The diagnosis of typhoid fever may be established by the demonstration of the specific causal agent—the bacillus of Eberth—in the body of the patient; by the demonstration of changes in the blood and tissue-fluids giving them specific, agglutinative properties, and by the recognition of a symptom-complex, characteristic of the reaction of the organism to the typhoid bacillus. Of these diagnostic methods—which we will term the bacteriological method, the serum method, and the clinical method respectively—the first is undoubtedly

[1] A well-marked and severe case occurred many years ago under my care in a vigorous old gentleman of eighty-two. By the labours of six nurses, working in pairs for eight-hour watches, he was brought to recovery, but only to die during convalescence of a diaphragmatic hernia.—ED.

the most assured, though the most difficult to carry out; the serum method has within recent years been largely utilised, and has proved a valuable, though by no means infallible aid in diagnosis; the clinical method of diagnosis still retains its premier position, and careful observation at the bedside will render it possible to come to a correct conclusion in the majority of cases.

1. *Bacteriological Diagnosis.*—The demonstration of the typhoid bacillus in the stools, in the blood obtained from a vein, from the rose-spots, or from the spleen, and its differentiation from allied organisms of the coli and enteritidis groups have been considerably facilitated by improvement in bacteriological technique. The method is, however, essentially a laboratory one and for the skilled bacteriologist, and provides for the certain elucidation of such cases as may be ambiguous or negative in their clinical aspects.

In the *stools* the typhoid bacillus has been demonstrated by His in 17 out of 21 cases in the febrile stage. The introduction of special media and methods has rendered the isolation of the bacillus more rapid and assured. Koch, during his investigation of the outbreak at Trier, was able to establish a diagnosis in twenty-four hours, and exceptionally as early as the second day of the disease. His investigations further showed that many cases of typhoid infection may occur with the specific organism in the stools without clinical manifestations, and particularly in children; a result which must have important bearings on the prevention of typhoid fever (see p. 1097).

Blood.—There is reason to believe that the typhoid bacillus is constantly present in the blood, and its isolation therefrom forms a valuable aid to the methods of diagnosis available at an early date. Collected statistics (p. 1087) show the existence of a typhoid septicæmia in 80 per cent of the cases examined. The blood is usually obtained from the median basilic vein by means of a fine syringe capable of holding some 8-10 c.c.; this amount of blood or half as much, obtained aseptically, is added to from 300-150 c.c. of nutrient bouillon and incubated. When typhoid bacilli are present, a growth is obtained in 60 per cent of the cases in from twenty-four to forty-eight hours; in other cases the growth of the organism is considerably retarded, even several days elapsing before it becomes manifest. In all cases it is necessary to establish the identity of the organism by further cultural procedures. In connexion with the delayed growth there is no apparent relation between the prognosis and the retardation. In many cases a positive result has been obtained before the serum-reaction appeared. Cultivation of the typhoid bacillus from the rose-spots has little or no diagnostic significance, as a well-marked eruption in itself provides a valuable criterion. Isolation of the typhoid bacillus from the blood obtained by splenic puncture has already been referred to (*vide* p. 1087). Adler makes the puncture with a fine needle thrust horizontally inwards for some 4 to 5 cm. at a point one inch below the upper limit of splenic dulness and in the mid-axillary line. From 1-10 drops of blood are withdrawn and

cultivated on bouillon. A positive diagnosis can generally be made in from ten to twenty hours.

Urine.—In occasional instances the isolation of the typhoid bacillus from the urine may be of diagnostic significance.

Serum Diagnosis.—The bearing of this reaction on the etiology of enteric fever has already been dealt with on p. 1085, and its value has been considered on p. 1093, where it was pointed out that the reaction is present in over 90 per cent of cases of typhoid fever, and that no symptom of typhoid fever is so constant as the serum-reaction (Delépine). The technique of the reaction is fully described on p. 692, and the agglutinins will be dealt with by Professor Ritchie in vol. ii.

Since the agglutination test is essentially a laboratory one, and involves the use of living cultures of the typhoid bacillus, it is not adapted for the clinician. Attempts to overcome this and to bring the test within the sphere of the practitioner have been made by the substitution of dead cultures; of such "Ficker's diagnostic" (37) is an example. Its value as a test has been confirmed by several writers.

2. *Clinical Diagnosis.*—Typhoid fever is often recognised without difficulty; sometimes the diagnosis can only be made after watching the symptoms for some days. It is during the first week of the fever that the chief difficulties are encountered, and here Wunderlich's propositions as to the temperature will be found a very useful guide; also such symptoms as severe headache, sleeplessness, and epistaxis. Ehrlich's diazo-reaction, though present in most cases, is also noticed in other febrile affections, and being often absent during the first week, is of no great help in doubtful cases. In distinguishing enteric fever from other affections we must note the temperature-curves, the intestinal symptoms, the characteristic rash, the enlarged spleen, and other less prominent symptoms. Thus in *typhus* fever there is the "typhoid" state, and there may be diarrhœa, but the fever is less gradual in onset; it remains high during the whole time of the fever, and on the fourteenth day there is usually a crisis and a rapid fall to the normal.[1] The rash in typhus appears earlier, generally about the fourth day, does not occur in successive crops, and persists to the end of the fever; the rash consists of spots of irregular form, red or dirty pink, which become reddish brown and then do not disappear on pressure, they often become hæmorrhagic, and they are more numerous and more widely distributed; besides the spots there is marked mottling of the skin of the abdomen. Violent delirium is much rarer in typhus than in enteric fever.

In *tuberculous meningitis* the temperature is rarely so high as in enteric fever with marked cerebral symptoms; the pulse if soft is no longer dicrotic, and may even be hard; persistent vomiting during the first few days occurs more frequently, and the abdomen is generally retracted.

[1] It is generally stated that in typhus the fever terminates abruptly in a crisis. According to Dr. Steell's observations this is not correct; the defervescence is gradual, lasting two days, and the fall of the pulse during the period of defervescence is also gradual.

Optic neuritis, whilst extremely rare in enteric fever, is not uncommon in meningitis; the same may be said of the inequality of pupils, and of squint. Tubercle of the choroid would be, of course, a pathognomonic sign, but it is not often present in the latter disease.

In *acute general miliary tuberculosis* we may have the history of previous cough or pleurisy; the temperature is not so high, the pulse is not dicrotic, the abdomen is retracted, roseola is rare, the examination of the stools may sometimes show the presence of tubercle bacilli, and emaciation is noticed early in the disease; yet in some cases the diagnosis is impossible. A roseolar rash may occur, though very rarely, in miliary tuberculosis; I have seen it in three cases—two at the Fever Hospital, and one under the care of my colleague, Dr. Steell, at the Manchester Infirmary. Diarrhœa and even intestinal hæmorrhage may be noticed, with tympanites and gurgling in the right iliac fossa, while the temperature may closely resemble that of typhoid fever (113). The much quicker pulse and the absence of dicrotism appear to me to be very significant distinguishing features in acute miliary tuberculosis, and also the aspect, which is usually alert and even excited; not oppressed, not apathetic, save towards the end; rarely even indifferent.

Tuberculous peritonitis may simulate enteric fever. I recall two cases admitted into the Monsall Hospital as enteric fever, in which for several weeks the symptoms much resembled it. In one of the two cases large tumour-masses in the abdomen could be detected about the fourth week of illness, and in the other case, after some weeks of pyrexia, fluid was discovered in the abdomen; in both cases the pulse was over 130 for many days.

The gastro-intestinal form of epidemic influenza may closely simulate enteric fever. We may have a roseolar rash (though this is very rare, and when it does occur is more widely distributed, and does not appear in successive crops), tympanites, gurgling (which, however, is not confined to the right iliac fossa), a markedly enlarged spleen, and profuse diarrhœa. The sudden onset of the fever, which often in less than twenty-four hours reaches 103° and 104° F., and the subsidence of the fever symptoms before the end of the second week, will help us to distinguish influenza from enteric fever, as will also the condition of the tongue and pulse. In some cases of influenza the pyrexia persists for several weeks, but diarrhœa and the other symptoms have then subsided (76). If there be cough with expectoration, the examination of the sputum for influenza bacilli, which can be easily recognised without any cultivation, will assist us materially to a correct diagnosis. I must, however, here observe that enteric fever and influenza may occur together. I have seen two undoubted cases of enteric fever immediately following an attack of epidemic influenza: in one the diagnosis was verified by a post-mortem examination, and in the second there was a distinct relapse after the enteric fever. Both cases occurred in adults; several members of the family were affected with typical influenza at the time, and in both cases a subsidence of the influenzal symptoms had taken place, when the

temperature again rose, and gradually all the prominent symptoms of enteric fever were manifested (*vide* p. 964).

We have already spoken of *pneumonia complicating typhoid*, and of *pneumo-typhoid*. There is, however, a form of pneumonia—*central pneumonia*—where the symptoms for a few days very closely resemble those of enteric fever. There may be no rigor, no pleuritic pain, the onset of the fever may not be sudden, and on physical examination of the chest no signs of pneumonia may be noticed for several days, that is to say, until the pneumonic process has reached the periphery of the lung.

Pyæmic and septicæmic affections, such as *infective endocarditis*, *osteomyelitis*, cryptogenetic *pyo-septicæmia*, and *puerperal septicæmia*, may produce a train of symptoms very much like those of enteric fever, including a roseolar rash, tumefaction of the spleen, and diarrhœal tympanites. Thus three members of one family had lived in a cellar-dwelling, which had been under water at a time of an extensive flood, and being attacked with febrile symptoms, they were sent to the Monsall Fever Hospital. Their symptoms closely resembled those of enteric fever, and one of them presented on the third day of admission marked roseolar spots, and had slight intestinal hæmorrhage on the fifth day; the temperature showed marked evening exacerbations; the patient died from exhaustion on the fourteenth day after admission (about the seventeenth day of the fever), and on post-mortem examination the intestines appeared healthy. I could quote several other similar cases. *Puerperal septicæmia* may sometimes be indistinguishable from enteric fever. Thus in a case reported by Leu a roseolar rash, tympanites, enlarged spleen, intestinal hæmorrhage, and a pyrexial curve like that of enteric fever were noted. In most cases of puerperal septicæmia, however, we notice, apart from any local symptoms, a high temperature early in the disease. There is from the first and often throughout the course of the disease vomiting and profuse diarrhœa; the pulse from the onset is quick, and not dicrotic; the spleen is found slightly enlarged from the first, and shows no further increase as the disease progresses; epistaxis and deafness are absent. The puerperal septicæmia often ends fatally after a few days—from four to ten days—or if recovery takes place, the fever symptoms subside at an earlier date than is the case in enteric fever. Some of the most difficult cases are those in which during or after some pelvic inflammation or mild septic poisoning enteric fever gradually supervenes as an independent event.

Acute gastro-intestinal catarrh may, if the fever be high, and remain so for a few days, as not infrequently happens in the young and in children, give rise to symptoms like a mild or abortive attack of enteric fever. The difficulties of diagnosis become especially great at the time of an epidemic of enteric fever, when many mild and abortive cases are about.

The *malarial* affections which occur in this country can scarcely be mistaken for enteric fever; in the remittent type of the severe malarial affections as they occur in tropical climates the presence of the parasite in the blood would form a pathognomonic sign.

Other affections with which enteric fever may occasionally be con-

founded are—*acute rheumatism* (especially during the first week of typhoid fever, when severe pains in the joints may be present), *mania, perityphlitis, hæmorrhagic colitis, pelvic cellulitis, epidemic cerebrospinal meningitis, extravasation of urine, acute trichinosis.*

In discussing diagnosis, we may remark that sometimes patients present themselves for treatment with symptoms of sequels of enteric fever, in whom the enteric fever had not been diagnosed. The case of intestinal obstruction quoted on p. 1100 is an instance in point, and other cases, especially some with prominent nervous symptoms, could be cited.

Prognosis.—Enteric fever, even in its mildest form, must be looked upon and treated as a serious disease; for even in mild cases death may occur from perforation, or from hæmorrhage, and sudden death without any premonitory symptoms, and for which no adequate cause can be found on autopsy, is occasionally seen. Perforation may occur during convalescence. As a relapse may occasionally be fatal, and as serious complications may occur during convalescence, the patient cannot be considered out of danger till convalescence is complete. We have, further, to bear in mind that however mild the fever may appear during the first and second weeks, grave symptoms are none the less likely to appear in the third week; no case therefore, however slight the symptoms at first, should be lightly treated. Some general propositions, however, may be stated as regards prognosis. As regards *age*, we may say that the older the subject the more unfavourable the prognosis: as regards sex, authors differ somewhat; according to many the affection is more serious in women than in men. The prognosis is less favourable in stout than in lean people, and very unfavourable in drunkards, in persons who have undergone great privation and fatigue (soldiers in war), in persons with weak or dilated hearts or who are affected with valvular affections of the heart, or who have incipient phthisis or diabetes; the prognosis is also grave in pregnant and puerperal women. In persons of marked neurotic disposition, acquired or inherited, the nervous symptoms and sequels are to be feared; and in those affected with renal disease aggravation of this disease and uræmic symptoms are apt to occur. Septic complications are to be feared in those who suffer from surgical diseases, especially suppurating wounds; and in those who live in unhealthy or insanitary districts. It is also well known that in hot weather the disease is often more serious than in cold weather. During the decline of epidemics of enteric fever, as in other infectious diseases, the cases become less and less serious. Certain families show a particular disposition to enteric fever; several members of the same family may be attacked at the same time, and other members readily contract the disease (see Pfeiffer, Wagner). Some years ago I saw two cases in the same family: in this family no less than five members had been attacked by it at various times; one contracted it by assisting in the laying out of the body of a relation who had died of enteric, and another had had it twice.

Apart from these general considerations, we are guided in our prognosis—

1. By the pulse: a slow, regular pulse indicates a favourable course; an irregular and intermittent pulse, even if not quick, is a grave omen, as it may denote myocarditis; a very quick and small pulse, except in young children, is an equally unfavourable sign, and if the pulse reach 140 or more in an adult, the issue is almost always unfavourable; a short and weak first sound at the apex of the heart, or disappearance of the first sound, is a grave symptom; a soft systolic bruit, limited in extent and not due to previous endocarditis, is of no special significance.

2. By the temperature: in young, strong subjects a high temperature, say 104·5°-105° F., if it only last for a few hours and rapidly fall to a lower temperature, and if the pulse be not very quick, is of no serious importance: if, however, the temperature remain high for some time, and especially if the fever be accompanied by nervous symptoms, and not quickly reduced by antipyretics, it is to be looked upon as very serious. Hyperpyrexia is a very unfavourable symptom, especially if after the application of cold the temperature does not fall much and rises very quickly afterwards; sudden fall of temperature, with the pulse remaining high, often denotes hæmorrhage or collapse.

3. By the nervous symptoms: low, muttering delirium, subsultus tendinum, convulsions (in adults), and incontinence of fæces and urine are of very grave omen.

4. By the intestinal symptoms: diarrhœa only becomes serious when it persists and is very profuse. Of the gravity of hæmorrhage and perforation we have already spoken.

Such complications as extensive pneumonia, pulmonary œdema, œdema of the glottis, hæmorrhagic nephritis, and symptoms of septic infection, are of serious import.

Special attention has been drawn to *sudden death* in enteric fever; it occurs in about 4 per cent of the fatal cases, and generally about the end of the third week. Excluding sudden or rapid death from perforation, changes sufficient to account for the sudden death have been found post-mortem in about two-thirds of the cases, such as embolism or thrombosis of the pulmonary artery, myocarditis, and degenerative changes in the myocardium; in about one-third no such changes could be found. Some think that death is due to syncope caused by reflex influence from intestinal lesions, others (Laveran) attribute the death to cerebral anæmia. The premonitory symptoms are sudden dyspnœa, irregularity of the pulse, and syncopal attacks (27).

Mortality from Enteric Fever.—Numerous statistics exist on this subject (see p. 62, and Table II. p. 1163). I will allude here only to a few of the more important points. The mortality per population has markedly decreased in England, but the mortality of the number of persons attacked with enteric, or (to apply a term used by continental observers) the mortality compared to the morbidity, is still for England as high as it was in Murchison's time, namely, about 17 per cent. From 1848

to 1870 it was 17·26 per cent, according to the return of the Registrar-General, and also according to the report of some of the larger fever hospitals (see table for Monsall Hospital return, p. 1164). In the Cork Fever Hospital the mortality (1871-1890) was 8·6 per cent; the mortality in the Glasgow Fever Hospital was 17·29 per cent. The statistics of some of the larger continental hospitals show a mortality slightly less than those of English hospitals; thus in Paris for 1882-88 it was 14·1 per cent, though since then it has risen to 20·6 per cent; in Berlin it was 14·5 per cent; in Leipzig (for 1880-1893), 12·7 per cent, whilst other places (such as Hamburg) show a much smaller mortality. To establish anything like a mean mortality in enteric fever is most difficult; it varies from year to year, and with the age and sex of the patient. Contrary to Murchison's views, most observers (Griesinger, Gesenius) are agreed that amongst very young children the mortality is high—Curschmann states it is least between the ages of two and ten years; in persons from ten to thirty years of age it is much less, but it increases again in persons over thirty. The mortality in the two sexes presents but slight differences, at times they are almost equal; in some epidemics the male mortality exceeds the female mortality, in others the reverse obtains, and any difference is due in men to external and social conditions, and in women to sexual functions. In a series of pregnant women (129) the mortality was 17 per cent, abortion occurring in 66 per cent; on the introduction of the cold-bath treatment it fell to 6 per cent, with 55 per cent abortions; in puerperal women the mortality is nearly 50 per cent. The mortality amongst soldiers, as given in the reports of the various military hospitals, is better fitted for statistical purposes, inasmuch as the reports deal with persons in the prime of life and living under the same conditions. The mean mortality (from 1875 to 1891) in the French army, as given by Brouardel, was 12·2 per cent, and during these seventeen years it only varied between 11 per cent and 14 per cent.

It is of great importance to know how far the various *methods of treatment affect the mortality*. To arrive at a satisfactory conclusion we must not consider results obtained from a limited number of cases in one locality or observations made during one epidemic. The evidence appears now to be conclusive that the hydrotherapeutic treatment carried out strictly after Brand's method has considerably lessened the mortality. Thus in the Prussian army the mortality fell from 25 per cent to 8 per cent, and in the various hospitals, in Germany, France, and America, where this system was rigidly carried out, equally satisfactory results were obtained (131). Thus—

	Per cent.
Drasche (Vienna) found a reduction from . .	16·2 to 9·3
Tripier and Bouveret (Lyon) found a reduction from	25 to 7·5
Osler (Baltimore) ,, ,, ,,	21·8 to 7·4
Thompson (New York) ,, ,, ,,	19 to 7

And lastly, Vogl (Munich garrison) gives the following statistics :—

	Per cent.
For 1841-1860	21
„ 1860-1875, treatment, partly expectant, partly by cold bath	15·2
„ 1875-1881-2, treatment by bath and combined . .	6·5

It must, however, be noted that the cold-bath treatment in some of the larger German hospitals has not reduced the mortality to so low a level as in the list given above.

The antiseptic treatment, so much recommended of late by some clinicians in England, has not as yet produced any marked diminution in the mortality of typhoid; but I do not know how far it is adopted in the larger fever hospitals. At the Monsall Fever Hospital at Manchester, where the mean mortality is about 17 per cent, the mortality fell during one year, when this treatment was extensively used, to 13 per cent; and some physicians, like Dr. Caton of Liverpool, dealing with a smaller number of cases, have recorded even a much lower mortality.

Treatment.—The possibility of a *specific curative treatment* for typhoid fever is becoming less and less remote, and although the attempts hitherto made in this direction cannot be regarded as having advanced beyond the stage of experimental inquiry, yet the results obtained are such as to give promise of future success.

Antitoxin Treatment.—Chantemesse (18) has prepared a serum for the curative treatment of typhoid fever, by the inoculation of horses with the toxins of the typhoid bacillus, obtained by growing it in a special medium, containing spleen-pulp and bone-marrow. Since 1901 Chantemesse has treated 545 cases, with a mortality of 4 per cent. During the same period 3199 cases of typhoid fever were treated in other Paris hospitals with the cold bath and the ordinary pharmaceutical preparations, with a mortality of 18 per cent. The results thus appear very encouraging. The serum, according to this author, exercises a rapid specific action, and the earlier it is administered the more marked is the effect. But the organism must possess the power of reaction; where the nervous system is already deeply poisoned the salutary effect is small, and failures occur. If the serum is injected before the eighth day in ordinary cases the disease may be cut short within a few days. Sometimes the first improvement is followed by a recrudescence; in such cases a second injection may be followed by rapid recovery. Injection of the serum is followed by a rise of temperature (reactive), which quickly falls again, the pulse is slowed, the urine increased in quantity. In the blood a leucocytosis is produced similar to that normally seen in convalescence from typhoid. Complications are rare in cases treated with the serum, though unless injected early in the disease the incidence of intestinal perforation is not diminished to such an extent as the other causes of a fatal termination. Among Chantemesse's fatal cases intestinal perforation accounts for one-third. The serum is injected under the skin of the forearm, with aseptic precautions. The ordinary dose is 10-12 c.c. A

second dose of 4-5 c.c. may be given at the end of eight or ten days, should there be a recrudescence of the fever. In cases coming under treatment early in the course of the disease the appropriate dose is 5 or 6 c.c.; in protracted cases with profound intoxication the dose should also be small, 5-8 c.c. In addition to the serum Chantemesse advocates the use of baths in high fever, and finds them more beneficial with the serum than with the usual pharmaceutical treatment. It may be necessary to stop milk-feeding for a time after the injection, as milk often appears to be ill digested; it may be resumed again as the temperature falls. No ill effects have been produced by the injections, except a slight erythema in a few cases. The encouraging results obtained by Chantemesse have also been confirmed in a small number of cases by Boutleux and by Josias.

Drs. A. Macfadyen and Rowland, triturating frozen (liquid air) typhoid bacilli and dissolving the substance in salt solution, obtained a highly toxic fluid, which on inoculation into horses led to the production of a serum having both antitoxic and bactericidal properties. As yet no records of the use of this serum in human patients are available.

Jez, on the basis of Wassermann's observation that the spleen, bone-marrow, and lymph-glands of an immunised animal had protective properties, prepared from these organs of immunised rabbits an extract which had antitoxic, but no agglutinative or bacteriolytic properties. In the treatment of typhoid fever this fluid is given by the mouth in doses of one tablespoonful every two hours, or more frequently; for each case a quantity of one pint or more is required. The therapeutic effects of this substance appear, from the few records available, to be worthy of further study. Jez, Kluk-Kluczycki, Eichhorst, Mesnil, de Rochemont, and Einhorn all agree that following the administration of this antitoxic extract the temperature falls, the pulse slows, loses its dicrotism, and the general condition of the patient is improved. Diarrhœa is usually checked. In some cases sweating is produced by the action of the remedy. Panetta, on the other hand, found Jez's extract quite useless.

Other observers, Widal, Bokenham, Krumbein, and Walker, have endeavoured to obtain a bactericidal serum by the inoculation of horses with dead cultures of the typhoid bacillus. Such serum acts variably towards different strains of the B. typhosus, most effectively towards the particular strain from which it was prepared. It is accordingly advisable to employ several varieties in the immunisation of the horse. The use of such antibacterial serum in the treatment of typhoid has so far met with little success; in fact, the indications, so far as they are known from the pathology of the disease, are to employment of antitoxic sera. Petruschky reports good results in cases of uncomplicated typhoid from the injection of small, gradually increasing doses of dead typhoid bacilli, which preparation he terms typhoin. This method, which is analogous to the tuberculin treatment of tuberculosis, does not seem to offer much probability of success.

Meanwhile, and until a specific remedial agent has been elaborated, our treatment must be directed towards the infected patient, with the idea of building up and maintaining in an efficient state the resisting powers of the tissues against the pathogenetic effects of the specific toxins.

In speaking of the treatment of enteric fever it is well to consider, first, the management of the patient as regards hygienic conditions, diet, etc., and then to review special treatment by drugs, baths, and so forth.

Hygienic Measures and Management of the Patient.—The patient should be put to bed as soon as the symptoms show themselves. The bedroom should be large, airy, and well ventilated; it should be in a quiet part of the house; it should not contain too much furniture, and should have no carpets or bed-hangings. It is well to have two beds in the room, so that the patient may be changed from one to the other; especially is this useful when the patient is treated with the cold pack. The patient should rest on a spring mattress, and a mackintosh be placed beneath the sheet; he should only be lightly covered, and the temperature of the room be kept between 60° and 65° F. In hot weather the temperature of the room may be artificially reduced. The patient should not be allowed to get up, and should be made to use the bed-pan; he should be as little disturbed as possible, and not examined oftener than necessary, the right iliac region in particular should be rarely and gently handled; to prevent hypostatic congestion his position should be changed. The trunk and limbs should be sponged with vinegar and water (at 85°-90° F.) night and morning; the mucous membrane of the mouth kept clean, and gargled with boracic acid, or with the following mouth-wash (Acid boracic ʒj., Potass. chlorate ʒj., Glycerini ℥j., Aquam ad ℥vj.), or the parts painted with boroglyceride; for the teeth the same wash may be used. Special care should be taken to prevent the formation of bed-sores, by washing the nates and adjacent parts with weak spirit or spirit of camphor. As soon as erythema appears, water- or air-cushions should be used, and the parts dusted over with boracic acid, or salicylic acid and prepared chalk. The patient should not be left alone, and if there be any active and violent delirium he should be treated with consideration and yet with firmness; he should never be strapped or otherwise fastened down, put into jackets, or otherwise restrained. In urgent circumstances, and for a short time, the sheet may be tightly drawn over him and fastened on both sides; but the proper means is to add to the number of the trained nurses. The window should be stopped so as to open no more than six inches, or a heavy table may be put in front of it.

Diet.—The diet should be nourishing, yet easily assimilable and non-irritating, and the food given often; the secretions of saliva, gastric juice, pancreatic juice, and bile being diminished, and the intestines ulcerated, great care is necessary in the selection of the diet. Milk is an excellent food in enteric fever; it is as a rule well borne, and should be given throughout the whole course of the illness. Two to three pints in the twenty-four hours is a sufficient quantity; patients will often take

more, but then the milk may be seen partly digested in the stool. The stools should be inspected, and the quantity of milk reduced if many curds are found. It is well to administer it diluted with lime water or soda water, or other aerated water, at intervals of about two hours. It may also be given in weak tea, or in the form of custard, or whey or junket beaten up with egg. When milk cannot be taken, peptonised milk, Benger's food, or arrowroot may be given instead (*vide* also p. 858).

Besides milk the patient may take mucilaginous soups, containing carbohydrates, which are of first importance, oatmeal, sago, rice, tapioca, wheat, aleuronat flour. Meat broths, such as chicken or mutton broth, beef-tea. Gelatinous substances, such as chicken jelly, calves'-foot jelly, and some of the other jellies. Proteid nourishment must be used with reserve; solid meat food of any kind should be strictly forbidden, but such proteid preparations as somatose, plasmon, sanatogen may be administered, or cold meat or chicken juice, made by macerating finely chopped lean meat or chicken in water; some hydrochloric acid and a little salt being added, and the whole strained through a cloth. Professor Osler strongly advocates the use of albumin-water, made by thoroughly shaking egg-albumin with ice and a small amount of water, straining, and flavouring with lemon, sherry, or brandy. If there be much diarrhœa, beef-tea or even mutton-broth had better be avoided. Fruit is inadvisable, especially if there be diarrhœa; but occasionally grapes, with skins and seeds removed, are much enjoyed and help to clean the tongue. As a *beverage* give pure water (which has been especially recommended in very large quantities by some writers) or barley water, or toast and water, or water containing the white of raw egg strained through a cloth: weak tea to which milk is added, or iced coffee may be given, especially when the stomach is irritable and the pulse flagging; aerated waters also may be allowed, except in those cases in which there are much flatulency and tympanites.

During recent years there has been a marked tendency towards an increased liberality in the feeding of typhoid patients, and many writers (Bushuyer, Shattuck, Wilson, Fitz, Moorhouse, Manges, Vaquez) have advocated the use of a soft solid diet even during the febrile period. In cases where there are no obvious contra-indications, and the patients express a desire for it, in addition to milk they may be allowed fish, minced meat, raw and soft-boiled eggs, macaroni, soft biscuits, toast, puddings, custard. Eichhorst, on the other hand, still advocates an exclusive milk diet until the third day of apyrexia.

Alcoholic stimulants need not be given unless there are special indications for them: such as failure of the heart, pulmonary œdema or congestion, insomnia, low muttering delirium, threatening collapse, or very high temperature. In tipplers stimulants are often necessary from the first, and should be given to avert some of the graver symptoms which so often threaten them. When the cold bath is given or the ice-pack, alcohol may be required before and after, especially if the patient be very weak or feel exhausted or faint. Alcohol is also needed when certain complications arise, such as perforation or hæmorrhage, which

lead to collapse. The best form of stimulant is brandy or whisky; the quantity depends on the age of the patient and the gravity of the symptoms; three to four ounces in twenty-four hours usually suffice for adults. When the pulse becomes small and thready much larger doses, even ten to twelve ounces or more, may be necessary. Alcohol should be given soon after some food is taken; or it may be taken in the milk every two or three hours; in critical cases every hour. Its effects should be watched and the large doses diminished as soon as the desired effect is produced; of this the pulse is the best index, which should become stronger and slower. When brandy is disliked we may give champagne or good claret. Alcohol should be withheld if signs of hæmorrhage from bowel or kidney appear, or if the urinary secretion become very much diminished.

Medicinal Treatment.—In mild cases, when the temperature does not exceed 102·5° F., no medicine may be needed; some physicians give small doses of hydrochloric acid and quinine, and if the patient come under treatment before the ninth day, several doses of calomel (gr. ij. to gr. v.) during two or three days. This administration of calomel, recommended by Wunderlich, Liebermeister, and others, appears to prevent a further rise of the fever, and to diminish the diarrhœa during the subsequent period; I have tried it also with good effect in the Monsall Fever Hospital. In the severer cases many physicians still follow an expectant treatment, and only treat grave symptoms such as marked pyrexia, profuse diarrhœa, as they arise; others follow a particular line of treatment, which in its conception is either *antipyretic* or *antiseptic*, or a combination of both.

Antipyretic Treatment.—We have various means of lowering febrile temperature, and I would distinguish particularly between the antipyretic treatment by means of the cold bath or allied methods, and that by means of antipyretic drugs.

A certain amount of pyrexia is an essential element in fever, and is looked upon by many persons as beneficial; it probably does interfere somewhat with the further growth, development, and action of the typhoid bacillus and its products, and it is said to increase the resistance of the organism. On the other hand, we know that a high temperature in itself is directly injurious to many organs, and occasionally the cause of severe nervous disturbances, though many of the grave nervous symptoms may occur with moderate temperature (*vide* p. 855). Most observers are agreed that a high febrile temperature requires active interference. Now the method of reducing the temperature is by no means a matter of indifference. Abstraction of heat without much diminishing the production of heat, which to a large extent is caused by the oxidation of the tissues and by increased tissue-metabolism, is the safest and best way of reducing the temperature; and the application of cold, especially in the form of the cold bath, best fulfils the requirements. There can be little doubt that whenever this treatment can be applied it is far preferable to antipyretic treatment by drugs; and a comparison of the mortality statistics of the

cases in which the cold-bath treatment is carried out, with those of cases in which antipyretic drugs are administered, clearly shows the superiority of the former method of antipyretic treatment (12 to 16 per cent compared to 6 to 10 per cent). Some of the best English clinicians, like the late Sir Wm. Jenner, are not in favour of the cold-bath treatment. Yet a glance at the tables published by the Registrar-General (*vide* p. 62), and by the several Hospital Boards in England, must satisfy every one that, whilst the mortality is much diminished, the mortality from enteric fever per case-rate in England, in spite of better hygienic conditions and management, is still very considerable.

The *cold-bath* treatment, first recommended by Currie of Liverpool in 1787, is now extensively used, especially on the Continent (*vide* p. 352). Its reintroduction is due to E. Brand of Stettin (1861), who showed how the mortality of enteric fever was lessened by its adoption; and his method was soon followed in a more or less modified form by other observers; in England Dr. Cayley most strongly advocated its use. Brand recommends it to be used whenever the temperature is over 102° F. (taken in the rectum), and this treatment he adopts from the very beginning.

Before the patient is put into the bath the face and chest may be sponged with cold water, and if the patient be weak and exhausted he receives some stimulant. The temperature of the bath varies from 65° to 70° F. The bath is placed close to the bed, and the patient is lifted into it and so immersed that the water covers the chest; the back of the patient is supported by a water-cushion, and a sheet or napkin is folded round the loins. The head and forehead are now covered by a cloth wrung out in cold water, and whilst the patient is in the bath cold water (of lower temperature than that of the bath) is applied to the head every three to four minutes, whilst the limbs and thorax are rubbed during the whole time of the immersion. While in the bath the patient has some cold water to drink. The duration of the bath is from ten to fifteen minutes as a rule; the patient is then lifted out and dried gently, except over the abdomen, put into bed lightly covered, and hot bottles are placed at the feet. A second dose of some stimulant, such as whisky and hot water, is then given to him. During the bath the state of the patient must be carefully watched; with the fall of the body-temperature he begins to shiver; but if the temperature before the bath has been very high, he may still be left for some minutes longer whilst the limbs and thorax are more vigorously rubbed. If the pulse be very weak, and the patient become cyanotic, he should be removed from the bath at once. After the bath the patient may take some food, and he generally then falls into a quiet slumber; if not, Brand recommends the application of compresses wrung out in cold water to the chest and abdomen. Half an hour after the removal from the bath the temperature is taken; it is usually found to have fallen 1° to 3° F., and if in two or three hours the temperature again exceeds 102·2° the bath is renewed. Brand has given as many as eight baths in the twenty-four hours, but usually four to six suffice. The good effects of the cold bath are readily seen: the pulse

becomes slower and the tension of the artery is increased, the number of respirations diminish, the tongue becomes moist, and the appetite improves; the nervous system is especially relieved, the delirium disappears for a time, the patient appears much calmer, and the sleep becomes more natural. The advantages claimed for the cold-water treatment are—that the fever runs a less protracted course, that grave nervous symptoms are less apt to occur, that the heart and pulse remain strong, that the tongue remains moist and the appetite good, and that the diarrhœa, if not lessened, is certainly not increased: statistics show that the mortality is less. The cold bath is contra-indicated when the pulse is irregular and intermittent, and when we suspect myocarditis or pericarditis; also in intestinal hæmorrhage occurring during the later stage, in peritonitis, and in old people. On the other hand, the puerperal state, pregnancy, bronchopneumonia, pneumonia, intestinal hæmorrhages during the first week, and albuminuria, are no contra-indications (Chantemesse). Relapses appear, however, to occur more frequently with the cold-bath treatment.

Brand's system of treatment is still carried out by a good many medical men, especially on the Continent. Many physicians, however, do not bath the patient unless the temperature reach 103° or 103·5°: many also advise the use of water of 80° F., the temperature of which is gradually lowered to 70° or 65°; this plan appears to have many advantages, and in some experiences it has given quite as good results as the stricter method of Brand.

In the Johns Hopkins Hospital at Baltimore each patient receives a tub-bath of twenty minutes at 70° F. every third hour, if the rectal temperature be at or above 102·5°. Prof. Osler says: "Two advantages are claimed for hydrotherapy in typhoid fever—a mitigation of the general symptoms of the disease and a reduction in the mortality. Our experience during the past five years bears out these claims." He adds that the beneficial action is "not so much special and antipyretic as general tonic and roborant. The typhoid picture is not so frequently seen." About 6 to 8 per cent more lives are saved. While continuing its use the author says that he prays for a method which, "while equally life-saving, may be, to put it mildly, less disagreeable."

The experience of F. E. Hare in the Brisbane General Hospital is very similar. With the introduction of rigorous Brand baths the mortality was reduced from 14·8 per cent to 7·5 per cent. He found it had no effect on the incidence of hæmorrhage or perforation or the fatality of these complications, and accordingly the reduction in mortality is entirely due to the beneficial influences of the cold bath on the pyrexia. This is strikingly illustrated by a comparison of the male and female case-mortalities. Hæmorrhage and perforation are more frequent in males, and the incidence of these is not affected. With the introduction of the cold-bath treatment the male case-mortality was reduced from 14·14 per cent to 8·7 per cent, the female case-mortality from 16·02 per cent to 5·6 per cent. Hirschfeld, at the same hospital, subsequently gave his experience of the

tepid bath, and with a smaller number of cases found the mortality further reduced to 3·4 per cent.

In certain cases it is well to place the patient in a warm bath, and to lower the temperature gradually by the addition of pieces of ice; these are cases of threatening syncope, or cases in which the breathing is very much oppressed from emphysema or laryngeal complications, or in which there is profuse sweating.

As the cold-bath treatment is difficult to carry out in private practice, other modifications of applying cold to the body have been recommended; such as the wet-pack, the ice-pack, sponging the body with iced water, or with cold water and vinegar, placing a cradle over the patient in which buckets containing pieces of ice are suspended (Fenwick), or Leiter's tubes, with iced water running through them, which are placed over various regions of the body, head, chest, or abdomen. None of these procedures, except perhaps the ice-pack, reduce the temperature so effectively as the cold bath.

Many physicians combine the cold-water treatment with medicinal treatment. Jurgensen recommends the cold bath when the temperature reaches 104°, and gives quinine. Liebermeister gives calomel when the patient is seen early; he recommends a bath of 70° F. when the temperature in the axilla is over 102·2° F., and, moreover, large doses of quinine (20 to 40 grains in the evening). Bouchard combines antiseptic treatment with the baths, but the initial temperature of the bath is only about 5° F. lower than the temperature of the patient, and is gradually reduced to 85°.

Partly as antipyretic, but more as hydrotherapeutic treatment, Dr. James Barr recommended *prolonged immersion in a tank bath*, 90-98° F.; later he modified the method and now advocates a continuous stream of tepid water to be played on the abdomen of the patient, who is suspended in a hammock.

In this country the cold bath or the tepid bath is still chiefly restricted to combating hyperpyrexia, though it is gradually being extended to the treatment of ordinary cases of enteric fever, to the displacement of the routine use of the antipyretic drugs. Quinine is still much used and is warmly advocated by Erb; it should be given in one or two large doses daily, and only at those times of the day when there is a natural fall in the temperature, that is, evening and forenoon: the dose for an adult should be from 15 to 30 grains, for a child 3-5 grains, or it may be given as recommended by Bouchard in four doses of 7½ grains, repeated at intervals of fifteen minutes in the evening of every third day during the first two weeks of the fever. Antifebrin (4-8 grains) and phenacetin (10-15 grains) are now much preferred to antipyrin (10-20 grains), as the latter may cause the temperature to fall too rapidly, and induce symptoms of collapse and irregularity of the pulse. Salicylate of sodium (15-30 grains) was formerly given largely in enteric fever. At the Monsall Fever Hospital some years ago the late Dr. Tomkins, then resident medical officer, tried salicylate of sodium in a very large number

of cases; but the depressing effects, the unpleasant accidents (such as delirium, vomiting, dyspnœa, etc.), and the tendency to hæmorrhage from the intestines which it produced, made us abandon its use. The antipyretics, antipyrin, antifebrin, and phenacetin are given when the temperature is over 103° F., and repeated after some hours when the temperature has again risen. A combination of phenacetin with 2-5 grains of quinine is now very much used. Apart from the therapeutic effect, it must be noted that a rapid fall of temperature after the administration of any of these antipyretics is as a rule a good prognostic sign. Among other drugs which were formerly preferred, but which are now rarely applied as antipyretics, are digitalis and veratria. Kairin and thallin have marked antipyretic properties, and thallin is still occasionally used.

Antiseptic Treatment.—Of the various antiseptic remedies *calomel* was the first to be used, and is still largely used by some physicians. It was not given in the first instance on account of its antiseptic properties, but because under its use the duration of the fever seemed to be lessened, and its course to be milder. Of its antiseptic virtue there can be no doubt, and experimental investigations have shown that it readily kills bacteria, that it prevents butyric acid fermentation,—a fermentation brought about by micro-organisms,—that it checks the formation of products of decomposition usually found in the digestive tract (indol, skatol), and that it does not interfere with the action of the unorganised ferments of the saliva, gastric and pancreatic juices (Wassiljeff). Occasionally its administration is followed by increased intestinal irritation. As Dr. Caiger remarks, it is chiefly of benefit in cases with severe headache, furred tongue, and constipation, and in such as have a tendency to abdominal distension with offensive diarrhœa early in the disease.

Perchloride of Mercury (½ to 1 drachm of the solution of perchloride of mercury, with 1 or 2 grains of quinine, given every four hours for several days) has been highly recommended by Sir W. Broadbent; especially when the motions are very offensive and accompanied by much gas, the abdomen much distended, and the fever high. Calomel or perchloride of mercury is only to be given for a few days; but recently more thorough antiseptic treatment has been advised, and numerous drugs have been recommended, not so much with the object of checking the action of the typhoid bacilli which have reached internal organs, as with that of acting on those still present in the intestines, and particularly of checking fermentation and the action of the numerous micro-organisms found in the alimentary canal, the growth and development of which are favoured by the presence of the typhoid bacillus, and the products of which may be absorbed through the ulcerated surface of the intestines.

One effect of the antiseptic treatment which is often apparent is that the dejections become less offensive, sometimes quite odourless; bacteriological examination of the fæces, however, shows that they still contain a very large number of living micro-organisms. Diarrhœa is often

diminished, the temperature reduced, and some of the graver nervous symptoms are said to be prevented. While some speak very highly of the effects of the antiseptic treatment, and record a very low mortality, others have seen but little benefit from the treatment. My own experience from a number of cases in which the various antiseptics have been tried makes me think well of this treatment, though it is certainly inferior to the cold-water treatment.

Of the various antiseptics which have been recommended we may mention—

β-Naphthol is given either alone in powders or capsules (5-10 grains every four hours), or mixed with salicylate of bismuth. 150 grains of β-naphthol are mixed with 75 grains of salicylate of bismuth and divided into thirty powders. From three to twelve of these are given in the twenty-four hours. Teissier recommends, besides, that four enemas with cold water be given daily to aid diuresis, and one enema containing 15 grains of quinine and an infusion of valerian (48). In cases in which constipation exists, *salicylate of magnesium* (50-100 grains daily) has been recommended.

Salicylate of Quinine I have often given (10-15 grains) with good effect.

Salol (40-60 grains in twenty-four hours) has come much into use of late. It is usually well borne, produces in these doses no toxic effects, deodorises the stool, and often relieves flatulence and tympanites.

Betol, or salicylate of naphthol, *naphthalin*, and benzoate of β-naphthol, or benzo-naphthol, have been highly spoken of by French observers. Hydronaphthol was recommended by Clark; magnesium benzoate by Klebs; dermatol (22) by other observers.

Carbolic Acid.—2½-3 grains in keratin pills, or in the following mixture (19), Acid carbolic liquefact. (Calvert) ♏xij., Tr. iodi. (B.P.) ♏xvj., Tr. aurant. ʒiss., Syrup simpl. ʒiij., Aquæ ℥viij.; ℥j. may be given every four hours for the first fourteen days, or till the urgent symptoms yield, and then three times a day (Moore), or *creasote* may be used, in pills or capsules, 1 to 2 minims; or paracreasotic acid (70).

Turpentine acts both as an antiseptic and as a stimulant, it checks tympanites, and is especially to be recommended in hæmorrhage. It must be given cautiously if nephritis be present. A dose of 5-15 minims given in capsules, or emulsified with yolk of eggs, I have often found well borne, or a mixture of the same with spirit of nitrous ether and spirit of chloroform (Moore).

Chlorine is highly recommended by Dr. Burney Yeo. Into a twelve-ounce bottle put 30 grains of powdered potassium chlorate, and pour on it 40 minims of strong hydrochloric acid. Chlorine gas is at once liberated. Fit a cork into the mouth of the bottle, and keep it closed till it has become filled with the greenish-yellow gas. Then pour water into the bottle, little by little, closing the bottle, and well shaking at each addition, until the bottle is filled. To 12 oz. of this solution 24-36 grains of quinine are added, and 1 oz. of syrup of orange-peel. Dose, 1 oz. every two, three, or four hours, according to the severity of the case.

Sulphurous Acid in 20 to 30 minim doses every two or three hours is capable of checking intestinal fermentation.

Camphor is recommended by Janeway; *Thymol* has been also used (126).

Essential Oil of Cinnamon in doses of 2 minims increased to 5 has been employed in a number of cases by Dr. Caiger and with favourable results; the temperature ran lower, the patients were more drowsy and restful, and intestinal fermentation was controlled to a striking extent.

Chloroform may be given internally, 1 part of chloroform in 150 of water (120, 136). Chloroform rapidly destroys typhoid bacilli.

Quinine must also be grouped with the antiseptic remedies.

Besides the antiseptic treatment of enteric fever we have yet to mention the administration of *potassium iodide*, which was very much in vogue on the Continent, as a remedy throughout the fever period, and is spoken of very highly; also the administration of large quantities of water by the mouth (104), or in the form of enemas: Cantario recommended large enemas of cold water and gallic acid (5 to 100 of water).

Treatment of special symptoms and complications.—I can only refer here to a few of the more important.

Hyperpyrexia.—All authors are agreed that there is but one plan of treatment for this event, namely, the cold bath. Where this is inapplicable, the ice-pack or cloths wrung out of iced water are to be applied to the limbs and trunk of the body, the cloths to be repeatedly changed till the temperature of the body is sufficiently reduced. At the same time large doses of quinine, 30-40 grains, may be given. This plan I found successful in two cases in which the temperature had reached 106·5° and 107° F. respectively.

For the *adynamic* form of fever subcutaneous injections of ether, caffein (subcutaneously or by the mouth, 1-3 grains), musk, or camphor may be used.

In the *petechial form* large doses of quinine, perchloride of iron, and lime juice are prescribed.

Constipation.—Constipation lasting only a few days, and not accompanied by much tympanites and flatulency, need not be treated medicinally; an admixture of beef-tea and milk diet may be tried. If the constipation be more obstinate, glycerin enemas or cold-water enemas may be given; should these produce little effect, and the constipation have gone on for five days or more, small doses of castor-oil (one to two teaspoonfuls in milk) may be given, and repeated after some hours if necessary.

Profuse Diarrhœa.—This may have to be treated if the alvine discharges amount to more than eight in the twenty-four hours, and if the patient is thereby rendered weak and exhausted. A starch enema, to which 20-30 drops of laudanum are added, often suffices to keep the diarrhœa within bounds, by diminishing peristalsis in the large intestines, and often the diarrhœa is due more to a catarrh of the large bowel than to the ulcerated state of the small intestines. Subnitrate of bismuth,

salicylate of bismuth, and mistura cretæ are equally efficacious; but if they fail one need not hesitate to give opium, either alone or in combination with acid (sulphuric acid preferred), or with acetate of lead or sulphate of copper. There is no objection to giving the opium with the lead or copper salt in the form of a pill; but it is better, perhaps, to give it in fluid form, so as to avoid mechanical irritation of the ulcerated surface in case the pill should not dissolve before it reach the affected part. As I have said, antiseptics, such as β-naphthol, often subdue the diarrhœa quickly.

Persistent Vomiting.—Food should be given in small quantities and often. Milk and lime water or Benger's food may be tried, or some of the prepared foods, or cold meat juice with acid. Bismuth in powder (10 grains) with cocaine hydrochlor. (gr. $\frac{1}{4}$), given three to four times daily, I have often found very efficacious. A sinapism to the epigastrium may also be applied. Ingluvin in 5 grain doses has been recommended.

Pain in the abdomen may be relieved either by cold or hot applications to the abdomen. The latter, either as fomentations or poultices, are highly spoken of by some English observers.

Tympanites.—Often a troublesome symptom. Enemas with turpentine or tincture of valerian often give decided relief. Turpentine may be given internally in capsules of 10 minims. If there be much flatulence, carbolic acid, creasote, or sulphocarbolate of soda (15 grains) may be tried. The application of ice to the surface of the abdomen is highly recommended by Dr. Cayley. If the tympanites do not yield to any of these drugs, the introduction of a long tube may give passage to much flatus; but this operation has to be repeated, as its effects are often very temporary.

Hæmorrhage from the Bowels.—We have already spoken of the gravity of intestinal hæmorrhage when it occurs after the first week, and when it is profuse. The patient must be kept quiet in the recumbent posture, and a small dose of morphine ($\frac{1}{4}$ grain) should be injected at once. Ice should be applied to the abdomen (the ice may be placed between flannel, or small pieces of ice may be placed in a kind of square dish made out of a piece of mackintosh). The patient should suck small pieces of ice, and all his food should be iced. Milk should be stopped, or given with carbonate of soda, or in the form of alum whey, that is, mixed with finely powdered alum and the curds separated from the serum (29). *Ergot* was formerly in general favour, but has fewer advocates now; it is best given as a subcutaneous injection of ergotin—1 to 3 grains. Of much more service are large doses of acetate of lead, given every two to three hours, or gallic acid and opium. Turpentine in 10 minim capsules (1 drachm given two to three times a day) has given me by far the best results. It is also contained in the mixture recommended by Murchison. (Acidi tannici gr. x., Tinct. opii ♏x., Spirit. terebinthini ♏xv., Mucilag. ʒij., Tinct. chloroform. co. ♏xv., Aquam menth. pip. ad ℥j.; this dose to be taken every two hours). Ice-water injections have also been tried with success. Opium enemas or morphine suppositories are to be

recommended. Adrenalin chloride has been employed, although it would seem that all the indications are against it; on the other hand, amyl nitrite has been recommended to induce general vaso-dilation. Calcium chloride in 10-20 grain doses every three hours is worthy of trial. Gelatin has met with no success.

The profound *anæmia* which accompanies or follows profuse hæmorrhage is best treated by subcutaneous injections of ether, and if the pulse become very frequent and small, a large quantity of normal salt solution is to be injected into the subcutaneous tissue. The salt solution is contained in a tin or glass vessel held or suspended at some height from the patient, and connected by means of an indiarubber tube with a fine aspirating needle; this is inserted under the skin below the scapula, where the subcutaneous tissue is loose. As the salt water flows into the tissue under a high pressure, a large quantity, half a pint or more, can thus be easily injected. The operation can be repeated on the other side after a little time. A very marked improvement follows the injection, though too often it is but temporary.

In peritonitis, whether due to extension of inflammation or to perforation, large doses of opium are given and poultices applied locally; if accompanied with symptoms of collapse alcoholic stimulants should be given freely, ether injected, and heat applied to feet and legs.

As *perforation* is almost always fatal if treated expectantly, surgical interference (that is, laparotomy, washing out of the peritoneal cavity, suturing the intestines, or the establishment of an artificial anus) is the only method to be considered. For success immediate laparotomy is essential. The only contra-indication is a moribund condition of the patient. (For statistics see p. 1121.)

Some of the various symptoms may require special treatment:

Persistent Insomnia.—Sulphonal or trional in 15-25 grain doses rarely has much effect. Chloral and bromide act better, but should not be given if the heart's action is weak; small doses of morphine may often be given with advantage, and without producing any ill effects; or paraldehyde.

Delirium.—Ice to the head, a sinapism to the back of the head, and morphine with quinine; if of low muttering character, stimulants may be given.

Delirium tremens is best treated by large doses of paraldehyde, and occasionally morphine may be necessary.

Weakness of the heart's action, indicated by the pulse, and due to change in the myocardium or to general prostration, is best treated by digitalis, ether, citrate of caffein, and by subcutaneous injections of strychnine ($\frac{1}{50}$ of a grain). Digitalis may also be given with advantage in the form of digitalin subcutaneously, or in granules, but its effects on the pulse must be watched. Von Ziemmsen recommends subcutaneous injections of camphor dissolved in olive oil (camphor 1 gramme, olive oil 5 grammes).

In acute dilatation of the heart, if it occur in plethoric subjects, and

especially if associated with pulmonary complications, cyanosis, and marked distension of the veins, venesection may be resorted to.

Bed-Sores.—These can be prevented by proper attention to the patient, as I have already said. The nurses should be able to lift the patient easily, he must not remain a moment wet or soiled, the buttocks must be washed (if danger threaten) once or twice a day with warm soap and water, and the skin disinfected with boracic acid and lanoline or other means. If the skin become rough, reddened, or show slight abrasions, the part may be washed with boracic acid solution or weak perchloride of mercury solution, and some ointment, such as zinc or boracic acid ointment, or iodoform powder, may be applied to the abraded part. If a slough have formed, antiseptic and stimulating dressings, such as carbolic acid (1 in 40), or compound tincture of benzoin, or balsam of Peru, are required. Over the lint, which ought exactly to fit the ulcer, a piece of gutta-percha tissue is applied, and outside this again some folds of lint, and the whole fixed by a strip of diachylon plaster. When the slough is large it is best to dust it over with iodoform, iodol, or aristol; this is covered by gutta-percha tissue, and over this lint dipped in an antiseptic or stimulating lotion is placed. The best preventive against bed-sores is to warn the head-nurse that she will be superseded if they occur. [See also article on "Nursing," p. 135.]

It would be beyond the scope of this article to speak of the treatment of the numerous complications and sequels of enteric fever, such as pneumonia, pleurisy, nephritis, as these subjects will be dealt with in the several articles on these affections.

Bacilluria.—For the manifest presence of typhoid bacilli in the urine, urotropin or helmitol 5 grains three times a day should be given for their proved antiseptic action.

Treatment during Convalescence.—Considering the nature of the lesion in enteric fever, and that the healing process can be but slow, the patient's progress during convalescence should be most carefully watched, and strict injunctions given as to rest, diet, and general management.

The temperature should still be taken for a fortnight, so as to judge of the progress of the case or foretell an impending relapse. The patient should keep to his bed for some days after the subsidence of the fever and till he feels sufficiently strong to get up; if there have been any heart symptoms he should keep to the recumbent posture even longer. Usually we may allow the patient to sit up for a short time about a week after convalescence has begun.

With the beginning of convalescence the stimulant should be at once reduced, and in young subjects may soon be stopped altogether. The diet for eight to ten days should still be chiefly of milk; soft boiled eggs may be allowed, and soups, milk puddings, and custards: if the diarrhœa continue during convalescence, even a longer period—about a fortnight—must elapse before the patient is allowed solid food; and then he should only be allowed to eat at first fish (whiting, sole), then such light food as chicken, pigeon, sweet-bread, tripe, before reaching beef and

mutton. Stale bread or biscuits, and a small amount of vegetables (rice, mashed potato) and stewed fruit may be allowed with the solid food. Drugs are rarely necessary during convalescence. If diarrhœa persist, bismuth, opium, and lead may be given; if, on the other hand, constipation occur, cold water taken in the morning fasting, or a cold infusion of senna-pods, or stewed fruit, will often overcome it: if these be insufficient, mild laxatives (Hunyadi Janos, Carlsbad salts, etc.) should be administered. When the patient's recovery is very slow, and he suffers much from anæmia and weakness, the mineral acids, with quinine or nux vomica, may be given, followed by mild iron preparations. Change of air materially helps to complete the convalescence, but the patient should not leave his home for a month after the subsidence of the fever, lest a relapse occur.

Prophylaxis of Enteric Fever.—Knowing the cause of enteric fever, the vehicles which convey it, and the factors which aid in its development, much can be done, and a good deal has been done, (1) to *check outbreaks of enteric fever*, and (2) to *prevent the spread of the disease.*

With the first of these two propositions sanitary science has occupied itself for many years and with very good results; many of the epidemics have been traced to a contaminated water- or milk-supply. Defective drainage and impure water may play an important part in the production of enteric fever, but they chiefly act by preparing, as it were, a favourable soil for the growth and development of the specific bacillus, and by rendering the body less resistant to its action. When enteric fever breaks out, it is advisable to boil drinking-water and milk, and to skin fruit before eating it. As in many places on the Continent the sanitary arrangements as to drainage and water-supply are still far from satisfactory, and as travellers and new residents are more apt to be attacked with enteric fever in places where enteric fever is endemic, than the inhabitants of the district, who appear to acquire immunity from it, it is well that travellers to continental towns should abstain from drinking water and unboiled milk, and when eating raw food should remove the skin of the fruit.

To prevent the spread of the disease, when it occurs in an endemic form, from the patient to those who come in contact with him, is no difficult matter if proper care be taken; for it is well established that the fæcal discharges and the urine are the only excretions which contain the active agent. Sputum, if there be any, should also be disinfected. The following measures should be adopted: the dejections (both urine and fæces) are to be received into a bed-pan containing a strong disinfectant (1-20 carbolic acid), and a sufficiently large quantity of the disinfectant is to be added to the discharge and well mixed with it. The nates must be well cleaned with paper, or with linen moistened with dilute carbolic acid; this refuse is burnt or added to the contents of the bed-pan. The bed-linen, blanket, and body-linen of the patient should be changed at once when soiled; they should be placed in a sheet soaked in carbolic acid (1 in 40), and afterwards kept for some hours in carbolic acid solution

of the same strength: before they are sent to the laundry they should be well boiled. The feeding utensils are to be cleaned in dilute carbolic acid, and afterwards with boiling water. The nurse, after attending to the alvine discharges or changing the linen, and always before she takes her meals, should wash her hands in corrosive sublimate solution (1 in 1000). Every precaution should be taken after the death of a patient as regards the bed-clothing, sheets, etc. Mattresses, pillows, and clothes should be sent to a disinfecting oven, when this is feasible.

Instead of carbolic acid as a disinfectant some use strong commercial hydrochloric acid or corrosive sublimate. Chloride of lime is an excellent disinfectant which quickly destroys typhoid bacilli, and it may be used to disinfect the fæces.

Anti-Typhoid Vaccination.—Following on the investigations of Pfeiffer and Kolle, Dr. A. E. Wright (138) has introduced a method of vaccination against typhoid fever. The vaccine used is a bouillon culture of several strains of the typhoid bacillus of high virulence, grown for four weeks and then sterilised by heating for ten or fifteen minutes at 60° C. The amount to be injected is the minimal lethal dose per 100 grammes of guinea-pig. The inoculations are followed by local redness and pain and some inflammation of the correlated lymphatic glands, faintness, nausea, and pyrexia. These reactive phenomena usually subside after 24-48 hours. The immediate effect of the inoculation is to diminish the resistance of the individual to infection by the typhoid bacillus (negative phase), followed later by an increase in the bactericidal and agglutinating power of the blood (positive phase), which may persist for at least two years.

This method has been tried on a large scale on British troops in India and South Africa, and although the validity of Dr. Wright's conclusions from the statistics so obtained has been questioned by Professor Karl Pearson, still there is with few exceptions a concensus of opinion that the vaccination affords a certain amount of protection against infection, that the disease, if contracted, pursues a milder course than in the non-vaccinated, and that its further employment as a prophylactic measure is desirable. Gaffky [46A] has recently endorsed the prophylactic action of this vaccine.

Julius Dreschfeld.

Paratyphoid Fever

In the following account of paratyphoid disease, clinical details are included so far as may be necessary for the purpose of showing the essential similarity of typhoid and paratyphoid fever. These infections are admittedly indistinguishable from each other except on etiological grounds, and the discovery of the latter disease as a member of the typhoid-colon group of infections was due solely to the bacteriological investigation of cases supposed to be instances of typhoid fever.

Within the last ten years a widespread form of infection with clinical features closely resembling those due to the bacillus typhosus

has been recognised. More detailed examination, however, shows that the bacillus present in the blood of these cases differs from the bacillus of Eberth, and that the agglutinating action of the serum is not that which occurs as the result of typhoid infection.

Clinical aspect.—More than 160 cases have been described by various observers, and the close similarity they bear to ordinary typhoid fever is obvious. The patient during the first three days suffers from vague symptoms of malaise and lassitude. On the fifth day the symptoms reach their height, and the patient passes into a "typhoid," stupid condition, with blunted sensibility. The cheeks are flushed, the eyes dull and sunken, and the conjunctivæ injected. Herpes labialis is sometimes present; the tongue is generally moist, but covered with a white coat. The abdomen at this time is rigid and slightly distended. The spleen is enlarged, but its free edge is rarely palpable. Often there is an eruption of red lenticular spots, which sometimes become confluent. Constipation is the rule. The temperature is between 102° and 103° F. in the evening, and falls about a degree in the morning. This continued fever is sometimes present from the outset, but is rarely maintained for more than a few days, and on the tenth to the twelfth day of the illness fever has disappeared; there is, as a rule, a fairly sudden onset of fever which runs a continuous course at a moderate height for several days; the temperature then becomes irregular, and rapidly falls by lysis. The loss of flesh is very marked. The disease lasts for a period varying between ten and twenty-four days, the average being fourteen days. Relapses occur in ten per cent of the cases, but they are less severe, and last for a shorter time than the primary attack.

The foregoing is an epitome of the ordinary clinical manifestations of the disease, but as in the case of typhoid fever there are various other forms. In one, resembling pyæmia, there are rigors and intermittent fever. The temperature shows wider oscillations, and may rise to 107·8° F. (42° C.) These cases may resemble malaria, and in the case described by Dr. Walker, the fever ended with excessive sweating. In another—the gastro-intestinal form — sudden shivering, followed by vomiting, characterises the onset, and there is abdominal pain, especially in the epigastrium and right hypochondrium. The temperature rises to 102° F. (39° C.), with morning remissions; there may also be vomiting and diarrhœa, the stools being very liquid and containing mucus and blood. This disease is, according to Kurth, the ancient "gastric fever." Another form, in which the patient is able to pursue his ordinary occupation, might be properly described as ambulatory paratyphoid.

The prognosis is favourable. Of the 162 cases described, 6 have terminated fatally.

As in typhoid fever, *complications* arise. Bronchitis and pleurisy have been recorded. Further, intestinal hæmorrhages occur in 5 per cent of the cases, but are much less important than in typhoid fever, though they may be repeated. Perforation, however, has never been recorded. Albuminuria is frequent, and there are recorded cases of

cystitis, pyelonephritis, and nephritis with blood and tube-casts in the urine. Finally, there is a striking number of complications of a suppurative nature. Furuncles are as frequent as in typhoid fever. Arthritis, osteomyelitis, suppurative osteitis, otitis, orchitis, cholecystitis, and hepatitis have been observed, and in nearly all these foci the paratyphoid bacillus was found.

Clinical investigation of the blood shows that the changes are very similar to those of typhoid fever. There is an absence of leucocytosis, and even a hypoleucocytosis has been noted. The mononuclear cells are increased during the period of infection. The eosinophil leucocytes are diminished at first, but are increased during convalescence. In cases where there is a leucocytosis, suppuration occurs. The investigation of the blood, however, by histological methods has been only very partially carried out.

Diagnosis—Every one of the symptoms of this disease may be met with in typhoid fever. Conradi, Drigalski, and Jürgens (183) give as the three most characteristic distinctions, which they had observed in the Saarbrücke cases, the favourable prognosis, the irregular temperature, and the long-continued convalescence. Such distinctions, however, are of no value in the diagnosis of a given case. At the outset the clinical characters point to a diagnosis of typhoid fever. The chief difficulty which presents itself is the failure of the Widal's reaction; but this is by no means universal. In any given case a clear reaction with races of typhoid bacilli may be obtained. In the Saarbrücke epidemic it was found that the reaction of the serum with paratyphoid bacilli was more quickly established, was present at higher dilutions of the serum, and lasted longer than that with typhoid bacilli.

Bacterial investigation of the blood or fæces is the most certain method of arriving at the correct diagnosis. The cases reveal the absence of the bacillus of Eberth, and the presence of a closely related bacillus. The paratyphoid bacillus closely resembles the bacillus of Eberth, both in its morphology, and in the sites in which it occurs. It has been found in the fæces, urine, bile, blood, the rose-spots, and in the exudation of a local inflammation or abscess. From the blood it is most easily isolated. A few c.c. are obtained aseptically from a vein, and are added to half a litre of broth, or placed in an incubator directly.

The characters of the *paratyphoid bacillus* are the following:—

Growth is aerobic; facultative anaerobic. It causes uniform turbidity in broth, without the formation of a pellicle, or of any odour. It does not form indol, and therein differs from the typical form of B. coli. It also differs from B. enteritidis, which, in spite of statements to the contrary, has, to a slight extent, the power of producing indol. It produces no coagulation in milk, but it clarifies it until it is almost limpid. The members of the Gaertner group have a somewhat similar effect on milk, but it is slowly produced. The growth on gelatin does not produce liquefaction, but is more vigorous than that of typhoid, and

assumes a pearly opacity. On plates the discrete colonies have the pin-head form, and differ somewhat in appearance from those of both B. typhosus and B. coli. On potato, the growth is intermediate in its appearance between that of B. coli and B. typhosus. The reaction of the potato is of great importance in determining the characters of the growth. The paratyphoid bacillus will grow on media after the growth of B. typhosus has taken place in it, but not after B. coli. On the other hand, B. coli easily grows on the old culture media of B. paratyphosus. On agar media coloured with neutral red, the paratyphoid bacillus causes a fluorescence in thirty-six hours. On the medium of Conradi and Drigalski large blue colonies develop which are very similar to those of B. typhosus. The bacillus grows well on the malachite green medium of Lentz and Tietz.

The bacillus has a high degree of motility. It stains by ordinary aniline dyes, and does not retain Gram's stain. Each bacillus has 8-10 flagella, which are shorter, more delicate, and less easily stained than those of B. typhosus.

Fermentation of Sugar.—With mannite and dextrose active fermentation takes place with the formation of bubbles. With lactose the fermentation is much slower than in the case of B. coli. With saccharose it is absent.

The majority of those who have investigated this disease recognise two varieties of the paratyphoid bacillus, A and B. Variety B is found in 80 per cent of the cases, and its characters are on the whole more like those of B. coli, while variety A is more allied to B. typhosus. Variety B grows more abundantly than A; is brown on potato; clarifies milk in a few weeks; produces bubbles of carbonic acid from 2 per cent lactose-broth; acidifies Petruschky's litmus-whey, which, however, at the end of the second week becomes alkaline; it forms thick opaque colonies on gelatin. Variety A grows less abundantly; is colourless on potato; produces little change in milk; forms no bubbles of gas from 2 per cent lactose-broth; does not make Petruschky's tubes finally alkaline, and forms clear, thin colonies on gelatin.

Immunity against B. paratyphosus is easily established. The animal immunised so that it can resist thirty times the fatal dose is at the same time immunised against one fatal dose of B. typhosus. A similar relationship exists with the bacillus of hog-cholera. It is a group immunity, but the degree is feeble. It has been suggested that in cases where the patient suffers from a second attack of typhoid fever the paratyphoid bacillus is responsible for one of the attacks. Similarly there is a group reaction of agglutination. The most remarkable case of this is recorded by Conradi, Drigalski, and Jürgens in their account of the Saarbrücke epidemic. In the case of one of the patients the serum agglutinated the paratyphoid bacillus at a dilution of 1 in 6000, and at the same time agglutinated a strain of B. typhosus at 1 in 5000. More commonly the serum causes agglutination of the B. typhosus at a low dilution, 1 in 50, while the reaction takes place with B. para-

typhosus at a much higher dilution (*e.g.* 1 in 1000). Again, cases occur in which only B. paratyphosus is agglutinated.

Morbid Anatomy.—There have been necropsies on several cases of paratyphoid fever. In some the intestinal lesions of typhoid fever were found, but there was no ulceration in most cases. The spleen is enlarged. The bacillus was isolated from the spleen, lymph-glands, and especially from the bile.

Again, the similarity to typhoid fever is seen in its etiology. It has been shown to be connected with drinking-water subject to surface contamination. Conradi describes a case in which the patient, a child of eight, had consumed some ice from water which was proved to contain both typhoid and paratyphoid bacilli, and in her fæces both bacilli were found.

Paratyphoid fever, then, is a disease which cannot be distinguished from typhoid fever either by clinical symptoms or by structural lesions. It would, therefore, seem necessary to regard enteric fever as a group of infections, including that due to the bacillus typhosus of Eberth, as well as that due to the bacillus paratyphosus of Achard and Bensaude. To determine in any given case the form of infection present it may be necessary to isolate the bacillus from the blood, urine, or fæces. The bacillus which, when isolated, agrees with all the cultural tests, may then be submitted to Pfeiffer's test in an immunised animal. Since this is more or less difficult to carry out, the much simpler agglutination test is, as a rule, adopted. To identify a bacillus, the serum of typhoid patients should not be used, but that of an animal whose agglutination power is highly developed, and is the result of subcutaneous or intraperitoneal inoculation.

The evidence derived from the agglutinating reaction alone of the patient's blood is not perfectly conclusive as regards the kind of infection. Numbers of cases have been published in which the test has apparently broken down. Zupnik and Posner (184) describe a group of five cases of fever in which the paratyphoid bacillus was agglutinated at the highest dilution. These cases were tested by Castellani's method, *i.e.* by adding agglutinable bacilli to the serum till its power was exhausted. The result was that three were exhausted by paratyphoid bacilli, and two by typhoid bacilli. Libman (185) has published a case in which post-mortem examination showed the presence of typical typhoid lesions. From the blood of the case the paratyphoid bacillus was isolated. The serum agglutinated the paratyphoid bacillus B at 1 in 50, and the typhoid bacillus at 1 in 250.

It is unnecessary to multiply cases of this type. The explanation may lie in some circumstance with which we are unacquainted. In the investigation already referred to on the cases of typhoid fever in the Belfast epidemic of 1898, Dr. Tennant and I showed that when the cases are studied by using a large group of typhoid bacilli, and not

merely by one which reacts well generally, it becomes clear that the reaction depends to some extent on the bacillus as well as on the serum. We found that certain races are relatively resistent to agglutination, while others are more susceptible to it. The same rule holds with the Gaertner and still more with the colon group. We selected from our races of B. coli a strain, isolated from normal fæces, which had, as far as could be ascertained, absolutely typical characters. We regarded this as a very suitable bacillus to use for inoculation for purposes of control, because we had absolutely failed to get agglutination with a 1 per cent dilution of any serum then in use. As a result of inoculation with this bacillus, a rabbit's serum became capable of agglutinating a typhoid bacillus at a fairly high dilution, but showed no effect on the inoculating bacillus. The explanation of at least some of the cases given above may be found in a study of the reaction from this point of view. Cases with anomalous reactions are, fortunately, rare in practice. If the test be carried out with typhoid, paratyphoid, and, if necessary, other varieties, *e.g.* Gaertner and B. coli, the great majority of cases will clearly show the predominance of the reaction to that kind of bacilli to which the infection is due.

J. Lorrain Smith.

APPENDIX

TABLE I.—Annual Mortality from Fever per Million Persons living.

Period.	England.			London.		
	Typhus.	Enteric.	Ill-defined.	Typhus.	Enteric.	Ill-defined.
1869	193	390	239	225	337	194
1870	147	388	233	147	303	177
1871	121	371	186	118	267	133
1872	80	377	145	52	242	97
1873	70	376	132	82	269	96
1874	74	374	130	91	256	98
1875	62	371	108	37	235	78
1876	48	309	81	45	217	57
1877	45	279	78	44	251	54
1878	36	306	71	41	283	54
1879	21	231	58	19	229	43
1880	21	261	58	20	186	35
1881	21	212	44	24	254	35
1882	36	229	39	14	252	24
1883	33	228	36	14	247	26
1884	12	236	28	8	284	20
1885	12	175	24	7	150	20
1886	9	184	22	3	154	18
1887	8	185	18	5	151	11
1888	6	172	15	2	169	9
1889	5	176	15	4	130	10
1890	5	179	13	2	146	9
1891	5	168	11	3	132	10
1892	3	137	8	3	102	5

TABLE II.—Death-rate from Enteric Fever per 1,000,000.

Year.	England.	London.	Manchester.[1]
1871	371	267	450
1872	377	242	400
1873	376	269	460
1874	374	256	390
1875	371	235	440
1876	309	217	420
1877	279	251	290
1878	306	283	310
1879	231	229	180
1880	261	186	260
1881	212	254	170
1882	229	252	250
1883	228	247	200
1884	236	234	190
1885	175	150	170
1886	184	154	290
1887	185	151	310
1888	172	169	330
1889	176	130	310
1890	179	146	270
1891	168	132	370
1892	137	102	240
1893	...	161	250

[1] The rates for the years previous to 1891 are for the Township of Manchester, and the Unions of Chorlton and Prestwich, which have been taken to approximately represent "Manchester."

Table III.—Enteric Fever: Monsall Fever Hospital,

August 26, 1884, *to August* 25, 1894.

Age.	Males.			Females.			Males and Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Under 5 years.	39	2	5·13	31	5	16·13	70	7	10·00
5 years and under 10.	151 moribund 1 152	8 1 9	5·29 5·92	151	9	5·96	302 moribund 1 303	17 1 18	5·62 5·94
10 years and under 15.	200 moribund 4 204	15 4 19	7·50 9·31	183 moribund 1 184	17 1 18	9·29 9·78	383 moribund 5 388	32 5 37	8·35 9·53
15 years and under 20.	274 moribund 4 278	38 4 42	13·86 15·10	150 moribund 1 151	29 1 30	19·33 19·86	424 moribund 5 429	67 5 72	15·80 16·78
20 years and under 25.	224 moribund 5 229	41 5 46	18·30 20·08	128 moribund 1 129	19 1 20	14·84 15·50	352 moribund 6 358	60 6 66	17·04 18·43
25 years and under 30.	144 moribund 1 145	40 1 41	27·77 28·27	98 moribund 5 103	18 5 23	18·36 22·33	242 moribund 6 248	58 6 64	23·96 25·80
30 years and under 40.	118 moribund 6 124	34 6 40	28·81 32·25	77 moribund 2 79	18 2 20	23·37 25·31	195 moribund 8 203	52 8 60	26·66 29·55
40 years and under 50.	39 moribund 3 42	13 3 16	33·33 38·09	40 moribund 3 43	14 3 17	35·00 39·53	79 moribund 6 85	27 6 33	34·17 38·82
50 years and under 60.	3	1	33·33	11	3	27·27	14	4	28·57
Over 60.	1	..	..	2	..	..	3	..	..
All Ages.	1193 moribund 24 1217	192 24 216	16·07 17·74	871 moribund 13 884	132 13 145	15·15 16·40	2064 moribund 37 2101	324 37 361	15·69 17·18

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RELAPSING FEVER

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SYNONYMS.—Famine Fever; Five or seven days' fever; Five days' fever with relapses; Remittent fever; *Typhus recurrens*; *Fièvre à rechute*; Epidemic fever of Edinburgh, of Ireland; Epidemic remittent fever; Relapsing synocha; Bilious relapsing fever; Bilious typhoid; Remitting icteric fever; Famine fever; *Die Hungerpest*; Miliary fever; *Typhinia*; *Homa el Rugga*, *Homa el Naxy*, or *Naushah.*

This fever, with enteric or typhoid fever, formerly confused with the larger group of typhous continued fevers, was separated and distinguished by a long series of researches and of observations gradually improving in accuracy in the first half of the nineteenth century. The essential character which distinguishes it from typhus is the occurrence of the relapse; while from enteric fever it is distinguished by the absence of intestinal lesions. The following brief description was given by Murchison:—"A contagious disease which is chiefly met with in the form of an epidemic during seasons of scarcity and famine. Its symptoms are: A very abrupt invasion marked by rigors or chilliness; quick, full, and often bounding pulse; white, moist tongue, sometimes becoming dry and brownish; tenderness at the epigastrium; vomiting and often jaundice; enlarged liver and spleen; constipation; skin very hot and dry; no characteristic eruption; high-coloured urine; severe

headache, and pains in the back and limbs; restlessness and occasionally acute delirium; an abrupt cessation of all these symptoms, with free perspiration about the fifth or seventh day; after a complete apyretic interval (during which the patient may get up and walk about), an abrupt relapse on the fourteenth day from the first commencement, running a similar course to the first attack, and terminating on or about the third day of the relapse; sometimes a second or even a third relapse; mortality small, but occasionally death from sudden syncope, or from suppression of urine and coma; after death no specific lesion, but usually enlargement of liver and spleen." With this description before us it is easy to see how relapsing fever might be confused with typhus, especially if cases of it were few; as the relapse might be either overlooked or attributed to some accidental or unexplained conditions. But when cases became more numerous the points of difference would, as happens during epidemics, be forced into prominence, and the more so that during certain epidemics sometimes cases of typhus proper would predominate, and sometimes cases of the fever with relapse. When also it appeared, by and by, that patients who had been affected by the one form of fever shortly afterwards contracted and went through a well-marked course of another, there could no longer be any doubt that two different kinds of fever were under observation. Henderson, of Edinburgh, was enabled in 1843 to advance arguments leading to the general acceptance of the view that relapsing fever must be distinguished as a separate disease from typhus fever. It appears now, in the light of further information, that relapsing fever is by no means a new disease. Spittal, of Edinburgh, stated in 1844 that Hippocrates described an epidemic of relapsing fever which he observed in the island of Thasos. The observations of Hippocrates are somewhat confused, some cases of doubtful character being described among others, which certainly appear to have been instances of relapsing fever. Neither then nor now did cases run a perfectly definite course; but the accounts would lead us to believe that in most cases the disorder ran its course in seventeen days.

History and geographical distribution.—As far as I am aware there is no reference to relapsing fever between the highly interesting records of Hippocrates and 1770, when Rutty described the weather, seasons, and diseases in Dublin from 1725 to 1765. It seems incredible that relapsing fever was absent during the long centuries that elapsed between these two dates, yet no references to its occurrence appear to be extant, unless, indeed, Strother, in his account of an epidemic which appeared in London in 1729, and Lind in his account of the contagious typhus of the fleet, both of whom speak of relapses, may be taken as referring to it. It may also have been seen in 1739, 1741, 1745, and 1748, since relapses were noted at all these times in the fevers rife in those years in Dublin. It was seen in Newcastle in 1777; also in Ireland in 1797-1801, and again in that country in 1817-19. In 1797-1800 the French doctors of Napoleon's army saw relapsing fever in Cairo; and Barbes pointed out that the jaundice, though accompanied by relapses, resembled the yellow

fever of America. Larrey, under the heading of "Yellow fever, complicating gun-shot wounds," describes a fever which succeeded the siege of Cairo in the spring of 1800. This may or may not have been relapsing fever. The chief symptoms were jaundice, fever, thirst, pain in the head and right hypochondrium, epistaxis, vomiting of bile, occasional delirium, and a marked crisis, sometimes followed by a relapse. When the city had fallen, the besieged garrison was found to be suffering from a similar disease, which probably consisted of both relapsing fever and infectious jaundice (Weil's disease). In 1826-27 relapsing fever was again seen in the United Kingdom, and now for the first time a distinction was drawn between two sorts of fever, which were no doubt typhus and relapsing fever, the former being far more fatal than the latter. Relapsing fever seems then to have disappeared from Britain till 1842, when it was seen in Scotland, and to a less extent in England. In 1843, 1846, 1847, and 1848 it continued to be prevalent; and in a diminishing extent was observed till 1852-54 both in London and Scotland. In 1846-47 it appeared in Upper Silesia and other parts of Germany. It was first seen in America in 1844, apparently revisiting that country again in 1850-51, and seems then to have disappeared till 1869-70, when an epidemic broke out in New York and Philadelphia at the same time that it was seen in the United Kingdom. According to figures kindly furnished to me by Dr. Tatham, of Somerset House, London, 139 deaths occurred in England from relapsing fever in 1869, 628 in 1870, 327 in 1871, 63 in 1872, and 41 in 1873. Since that time the mortality from relapsing fever has been trifling. For the thirty years ending 1903 the total number of deaths registered in England and Wales as due to relapsing fever was only 366, or an average of about 12 a year. In the last five years only 14 deaths have been registered from this cause. It seems doubtful even if all the deaths registered in England were really due to it, because a considerable proportion of them is set down as occurring under five years of age. For instance, in the years 1878-92, 182 deaths were registered in England and Wales as due to relapsing fever, and of these 24, or about 13 per cent, were said to have occurred under five years of age, a time of life at which relapsing fever is very rarely fatal. It seems much more probable that these deaths were due to some other forms of infantile fevers than to relapsing fever. In Scotland there do not seem to have been any cases of relapsing fever seen for a generation; and in Ireland I am informed by the Registrar-General for that country that only 40 deaths have been registered as due to that disease from the time when, in 1881, relapsing fever was first classified as a cause of death, till the end of 1903, a period of twenty-three years. For the last thirty years, therefore, we may say that relapsing fever has been practically absent from the United Kingdom; although, considering the long periods of time during which it has disappeared on former occasions, its long absence by no means renders us safe from further visitations. Relapsing fever is still epidemic in Egypt, and is more common in Lower than in Upper Egypt, or than it is in the Soudan (Sandwith).

This may be due to the less elevated temperature of Lower as compared with Upper Egypt, or on the greater density of its population. It very rarely attacks Europeans. Out of many hundreds of cases seen by Dr. Sandwith, only one occurred in a European, an English doctor who had been treating a case of uncertain nature, which afterwards proved to be relapsing fever. During the eleven years ended with 1904, Dr. Sandwith had 35 cases admitted to the hospital at Kasr-el-Ainy, but in 3 out of the 11 years no case was admitted. Most of the hospital cases appear to have been men, but in the villages plenty of women were affected, and in some villages there were more female than male cases. It still sometimes exists in provincial Egyptian prisons, notwithstanding hygienic improvements, but it is not known in the English or Egyptian armies (Sandwith). In India the disease occurs from time to time, and often in a very severe form, a mortality of no less than 18 per cent having been experienced from it in some epidemics. In St. Petersburg, in 1865, the mortality was also high, 14·9 per cent. The immunity of European residents in Egypt is referable probably not to peculiarities of race, but rather to the favourable circumstances in which they live as compared with the poorest natives. Starvation does not seem to be an important cause in Egypt, since relapsing fever did not occur among the starving refugees during the Mahdi's rule in the Soudan. Hard work, does, however, appear to be a disposing cause, for in the Tourah prison epidemic, where all the convicts were similarly treated as regards overcrowding, ventilation, and dirt, 74 per cent of those working in the quarries at heavy labour caught relapsing fever, in spite of their extra diet; while the light-labour convicts, such as basket-makers, carpenters, cooks, and water-carriers, only furnished 26 per cent.

Etiology.—*Remoter Causes.*—So far as I saw, the male sex was much more liable to relapsing fever than the female. Murchison gave the proportion as 116 to 104, but inclined to the opinion that sex had very little influence. If the male sex suffer more than the female, it is probably because men are more exposed to the infection. As to age, relapsing fever (like other fevers) is especially a disease of early life. Most of my cases occurred in young male adults. Murchison gave the mean age as 24·4 years. As to occupation, almost all the cases were either among paupers or the very poor. This has been the general rule in epidemics of the disease, and is so notorious as to have given a name to the disease. At the same time, it must be said that careful inquiry in Bradford often failed to show that the sick had undergone any special hardships or privations in food. Trade was then moderately good in the town, and the consequent demand for labour was pretty active. In Liverpool at the time of the epidemic of 1870, according to the *Lancet* report, "there was full employment for every able-bodied and industrious man." The patients themselves did not show any signs of want of food. Of 522 patients of whom the inquiry was made, only 91 had been in the workhouse before, which shows at least that they did not belong to the habitual pauper class. Besides this, at the time of the Liverpool

epidemic, there were (1) considerably fewer inmates in the workhouse, (2) considerably fewer families in receipt of outdoor relief, (3) considerably fewer patients suffering from zymotic diseases than in the corresponding period of the year preceding. From all these circumstances it appears as if the name of "famine fever" is not always appropriate. Other circumstances appear to enter into the causation of the disease. Mere overcrowding is not a sufficient cause, as some very overcrowded populations have suffered even less from it than others less densely packed. The *Lancet* report on the Liverpool epidemic in 1870 showed that there were at least three principal causes, namely, (*a*) the sites of the houses, which were frequently placed on decaying vegetable and animal matter and midden refuse ; (*b*) insufficient and imperfect drainage; and (*c*) the extensive prevalency of cellar-dwellings in darkened and filthy courts.

On the other hand, much evidence exists to show that there is as a rule some connexion between the occurrence of relapsing fever and the existence of destitution among the population attacked. Contagion cannot explain the whole of the cases or the spread of epidemics. Not to mention that in Bradford and Liverpool in 1869-70 the mass of the cases of the disease occurred among the pauper class, Murchison showed that in London 97·5 per cent of the cases investigated by himself were paid for by the parochial authorities, and were totally destitute. Nine of the remaining cases (430 in all were investigated) were admitted free, and were also destitute. Not a single patient had been a servant in a private family, and in one instance only was a fee for admission paid by the patient's friends. It is probably, also, not without significance that the epidemics of 1817, 1818, and 1819 raged during a period notorious in British history for low wages, high prices of food, and general depression due to the fall of the inflation of the markets caused by the great continental war; while the epidemics of 1843-44 and of 1847-48 occurred about the time of the great Irish famine. In 1826 Stokes described relapsing fever as famine fever, and in 1847 Corrigan's pamphlet bore the title, *On Famine and Fever, as Causes and Effect in Ireland.* During the epidemic in Silesia, in 1847, the inhabitants, in consequence of a succession of bad harvests, had been reduced to subsist on clover, grass, mushrooms, and the roots of trees. The synonym "Hungerpest" points unmistakably to the connexion, in German opinion, between relapsing fever and the existence of destitution. "Carter states that it was brought to Bombay in 1877 by the peasantry flocking into the city from famine-stricken districts" (Fagge). Murchison's view, as is well known, was that relapsing fever is due to destitution, while typhus is produced, he thought, by overcrowding and destitution combined.

Immediate causes—contagion.—The question of the contagiousness of relapsing fever was very fully gone into by Murchison, who proved his position that it was an exceedingly contagious disorder in the same way that he did for typhus fever. Several points in corroboration of his

opinion came under my notice. Thus several cases were admitted to hospital from the same house or street, and the circumstances left little or no doubt that some patients had been infected by others. In one case, again, early in the epidemic, and before I was accustomed to recognise the fever, I ordered a patient suffering from it into the general ward, thinking he had rheumatism. It was not long before I had to order both his removal and that of another patient, who lay beside him, to the fever hospital. Both had relapsing fever, and the other patient had been some time in the general ward. However, no nurses or attendants on the sick in Bradford took the disease from patients. I suppose this good fortune was due to the number of our cases not being very large, and also perhaps because our fever hospital was roomy and airy, rather than that our cases were not so infectious as in other epidemics. At any rate, both in 1818 and in 1843 relapsing fever appeared as a very infectious disorder. Thus Welsh says of the epidemic of 1818, that in the course of four months his three colleagues, two of the young men in the apothecary's shop, two housemaids, and thirteen or fourteen nurses, caught the disease; and the matron and one of the dressers died of it. In Queensberry House in 1818 two medical men, the matron, two apothecaries in succession, the shop boy, washerwoman, and thirty-eight nurses were infected, and four of the nurses died. Of the epidemic of 1843-44 Wardell wrote: "Most of the medical officers connected with the Edinburgh Royal Infirmary and additional fever hospital were seized with it; eight of the resident and clinical clerks in quick succession became affected. . . . The majority of the nurses and domestics took the disease, and of the former, at one time, no less than nineteen were labouring under it." And more to the like effect. Begbie, from his experience of the epidemic of 1847, arrived at the conclusion that relapsing fever, like typhus, was communicable from "the sick to the healthy; that for this purpose actual contact with the sick was not necessary, the subtle poison of this form of continued fever, equally with that of typhus, being readily conveyed through the air surrounding the latter; and, lastly, that by means of fomites or clothes the disease may readily be propagated."

According to Dr. Sandwith the liability of attendants on the sick and others to contract relapsing fever was well seen at Tourah. Volunteers, at the rate of one convict to ten sick, were taken from the healthy prisoners to act as ward attendants, and out of 74 of these, 39 caught relapsing fever after periods of time varying from two to six weeks. In addition, the director of the prison, five warders, two clerks, and four of the black sentries were attacked. None of the laundry workers, however, contracted the fever; and though several, including Dr. Sandwith, cut their fingers at autopsies of relapsing fever patients, they all escaped.

A. R.

Bacteriology.—The cause of relapsing fever is the micro-organism first seen in 1868 by Otto Obermeier, and called after him Spirochæta

Obermeieri. He described it (1873) as a fine, twisted, thread-like microbe, exhibiting, in a high degree, the phenomenon of motility, and as occurring in the peripheral blood only during the pyrexial paroxysm. The constant presence of this microbe in cases of relapsing fever was soon made out by Münch, Lebert, Birch-Hirschfeld, Heydenreich, and others; and its causal relation to the disease became apparent when Münch, Moczutkowsky, and Metchnikoff showed that the injection of spirochætal blood causes characteristic relapsing fever in normal individuals. Similar results were obtained by Vandyke Carter and Koch, in the case of certain catarrhine monkeys. In the last fifteen years the main problems studied have been in connexion with the biology of the microbe and the means by which the infected host gets rid of it. In this line of work the most important studies have been those of Russian pathologists, notably Metchnikoff, Gabritschewsky, Sawtschenko, and Melkich. The most interesting modern development of the spirochæte problem is, however, to be sought in the work of Fritz Schaudinn, who has brought forward incontestible evidence that Obermeier's spirochæte is an animal parasite, and not a schizomycete, as it was formerly believed to be.

Morphology of S. Obermeieri.—The spirochæte, or, as it is frequently called, the spirillum of relapsing fever is a fine, spirally-wound thread, slightly pointed at the ends and measuring about 15-40 μ in length by ·3-·5 μ in width. No details of structure can be made out even with the highest magnifications, the microbe appearing perfectly homogeneous. Certain variations from the typical form have, however, been described at various times, although nothing is known about them with certainty. Karlinski and Afanassiew have described rounded and rod-shaped micro-organisms in the blood of patients suffering from relapsing fever, but the significance of these is uncertain. One of the most striking features of the spirochæte is its extraordinary motility, which has been the subject of detailed study, especially by Heydenreich. At least three motions occur: (1) rotation round the long axis of the thread: (2) undulatory (backward and forward) movements of the whole thread;. (3) lateral movements in all planes. The mechanism by which these movements is carried out is unknown, although it has been suggested that they may be brought about by a fine undulating membrane such as occurs in certain Protozoa. At any rate, observers are unanimous that it is impossible to demonstrate the presence of flagella. The greatest degree of motility is manifested during the febrile paroxysm, the microbe gradually slowing down as the crisis approaches. The spirochæte is easily stained by watery solutions of basic anilin colours, and by Romanowsky's method and its modifications. It is decolourised by Gram's method.

Relation of the spirochæte to the phases of the disease.—As mentioned above the spirochæte is found in the peripheral blood only during the pyrexial paroxysm. Towards the crisis and during the critical sweat it disappears, to appear again with the onset of the relapse (Obermeier, Lebert, Ewald). The exact times of its appearance and disappearance

present certain variations; and Naunyn has in one case observed the continuance of the parasite in the peripheral blood during the entire period of apyrexia. In general the appearance of the parasite corresponds with the onset of the febrile paroxysm, or actually after it has begun. Heydenreich, Carter, and others have, however, seen it in the blood before the initial rigor. The number of parasites bears no relationship to the clinical severity of the case. For a long time it was supposed that the blood of the cadaver was devoid of spirochætes, but modern staining methods have shown that this is not so. Where death has occurred during the paroxysm the parasite can be found in the blood. If death ensue in the apyrexial period, the organs are free of the parasite, with the exception of the spleen (Metchnikoff, Soudakewitch, Nikiforoff). Intra-uterine infection of the fœtus has been seen several times with or without enlargement of the spleen (Albrecht, Spitz, Mamurowsky). The spirochæte is found only in the blood. It has been sought in vain in the urine, milk, fæces, sweat, conjunctival secretion, hydrocele fluid, pus, and the fluids from medicamentous vesicles. Although present in the hæmorrhages which may occur during the disease, its presence in menstrual blood is doubtful.

Behaviour of the spirochæte in blood outside the body.—Obermeier himself found that the spirochæte can live in blood *in vitro* for eight hours. A great deal, however, depends upon the manner in which the blood is conserved, and the period of the disease at which the spirochæte was withdrawn. Gabritschewsky found that when the blood is drawn during the first two days of the paroxysm, the extra-corporeal existence of the parasite was, on the average, 147 hours, the death of the spirochæte being estimated by the cessation of its movements. Heydenreich has shown that the spirochæte lives longest outside the body when the blood is kept at room-temperature (15-20° C.). The following abstract from his experiments shows his principal results in this connexion:—

Low temperatures	(− 10° to − 18° C.)	spirochæte survives	up to 8 hrs.
„	„ (− ·6° „ + 7·5° C.)	„ „	9 hrs. to 3 days.
Room	„ (+ 15·5° „ + 22° C.)	„ „	2½ to 14 days.
Body	„ (+ 37° „ + 38° C.)	„ „	15 to 21 hrs.
Febrile	„ (+ 39·5° „ + 41·7° C.)	„ „	4 to 12¾ hrs.
Hyperpyrexial	„ (+ 42·5° „ + 46° C.)	„ „	1¾ to 3½ hrs.

Action of chemical substances on the spirochæte.—Although a large number of experiments have been made upon the action of chemicals on the spirochæte *in vitro*, the results are unsatisfactory, chiefly on account of the great variability in the number and vitality of the parasites. The rapidly fatal effect on the spirochæte of solutions of quinine, strychnine, salicylic acid, potassium iodide, and so forth show that experiments outside the body are inconclusive, as such drugs are entirely without effect upon the parasite in the living body.

In 1890 Pasternatzky showed that it is possible to keep the spirochæte alive for some time in the body of the leech. He found that

when kept at a temperature of 16-17° C. the spirochæte remained alive up to four days, and when kept in ice up to ten days from the date on which the leech was allowed to suck spirochætal blood from a human being. Karlinski found the spirochæte still motile in the leech, up to twenty days. The duration of the parasite's vitality in the bed-bug is considered later. All attempts to cultivate the spirochæte on ordinary bacteriological media have proved fruitless.

Experimental Relapsing Fever.—(I.) *In man*—(*a*) Intentional inoculations. Münch inoculated himself with blood containing the spirochæte, and passed through a severe attack of the disease. Moczutkowsky (1876) repeated the experiment upon normal individuals with a like result. He further showed that the spirochætes found in the blood of cases of Griesinger's "bilious typhoid" can set up ordinary relapsing fever. On March 5 and 7, 1881, Metchnikoff inoculated himself with spirochætal blood, and became ill on March 12, passing through a characteristic attack with two relapses. Inoculation with blood taken during apyrexia is negative. (*b*) Accidental inoculations have also led to the disease. Well-known cases are those of Perls, who wounded himself during the autopsy of a case of relapsing fever, and developed the disease. Baschenow (1892) cut his finger with a cover-glass smeared with blood from a case of relapsing fever, and after an incubation-period of seven days, went through a characteristic attack (Wladimiroff). Of great interest are the two attacks which befell Vandyke Carter. The first took place on December 9, 1877, and resulted in a severe infection with one relapse. He had scratched his finger while making an autopsy on a patient, who died during the critical fall of the first relapse. He was again infected on February 16, 1880, showing fever on February 23 at 3.30 P.M. An assistant at the same autopsy was attacked with fever on the same day at 3 P.M.

(II.) *In animals.*—As far as is known only monkeys are susceptible to the Spirochæta Obermeieri. Dogs, cats, rabbits, pigs, sheep, rats, guinea-pigs, mice, horses, pigeons, fowls, and geese have been inoculated without success. Since the original reproduction of relapsing fever by Vandyke Carter and Koch in monkeys, these animals have been the subject of a great deal of study, and many important points in the pathology of the disease have been elucidated. Various species of monkeys have been used, but especially Macacus (*M. rhesus*, *M. javanus*, *M. cynomologus*), Semnopithecus, and Cynopithecus. In Carter's twenty-one experiments a positive result was obtained in 71 per cent. The incubation-period lasts 30-126 hours, the variation apparently depending on the severity of the infection and the phase of the disease at which the blood was taken. At the end of the incubation the disease in the monkey breaks out acutely, the acme of the febrile paroxysm being reached in a few hours. The whole paroxysm is shorter than occurs in man, and although as in him the fall of temperature is critical, there is no sweat. Relapses are much rarer than in man, and in any case the symptoms are less severe than in the primary paroxysm.

Infectious nature of relapsing fever and mode of exit of the spirochæte from the human body.—Numerous observations show that relapsing fever is contagious, the older belief being that the poison of the disease was conveyed through the air (Murchison). The spirochæte is an obligate blood-parasite, and does not escape from the body in the secretions or excretions. Years ago Klebs suggested that it might be conveyed by some animal parasite, and in recent years this has been made almost a certainty by the researches of Tictin and Karlinski on the bed-bug (*Cimex lectularius*). Tictin placed fasting bugs upon patients during the febrile paroxysm, and also on monkeys suffering from the disease, and he was able to recognise the spirochæte up to 77 hours. He also succeeded in infecting healthy monkeys with fluid taken from squashed infected bugs. In Bosnia Karlinski examined a large number of bugs from infected dwellings, and found the spirochæte constantly. He states that it can live in the body of the bug for as long as thirty days. It is suggested that the mode of infection is either the direct introduction of the spirochæte by the bug, or that the bite leads to scratching or the actual capture of the bug, and in this way the patient infects himself from contaminated fingers.

Pathogenesis of relapsing fever.—The cause of the disappearance of the spirochæte from the peripheral blood during the apyrexial remissions has been the subject of much speculation. Heydenreich, one of the earliest investigators of this problem, thought that the parasite perished as a result of the precritical rise in the temperature. Against this view it may be urged that the precritical temperature is not always high, that the spirochætes increase up to the time of crisis, and that the spirochæte may withstand a temperature of even as high as 48° C. Other hypotheses, assuming that the spirochæte is destroyed in virtue of the concentration of the blood-plasma (Moczutkowsky), or that there is a heaping up of metabolic products (Albrecht), have in recent years been discarded as insufficient to account for the phenomena observed. Since 1887, when Metchnikoff demonstrated the existence of phagocytosis in the spleen during the apyrexia, this factor has been regarded as an important one in explaining the disappearance of the parasite from the blood. Metchnikoff looked upon the spleen as the great defensive organ employed by the host to rid itself of the spirochæte, and his experiments seemed to have found a remarkable support in those of Soudakewitch (1891), who compared the effects of the spirochæte in normal monkeys (*Cercocebus fuliginosus*), and in those which had been splenectomised at a period anterior to the infection. While the normal animals recovered, the splenectomised monkeys succumbed in 8-9 days, with enormous quantities of spirochætes in the blood. It may be added, however, that Tictin (1894) failed to confirm these observations, and while admitting that spleenless animals resist the infection with greater difficulty, he could find no essential difference in the two cases. He found also that a certain degree of immunity is acquired by normal monkeys as a result of the infection, and that such immunity is not destroyed by a subsequent splenectomy.

In recent years the part assigned to the phagocytes has been minimised by the discovery of Gabritschewsky that there exist in the serum spirillicidal substances which produce immobilisation, spherulation, and destruction of the spirilla, apart altogether from any co-operation on the part of the fixed or wandering phagocytes. By mixing serum containing spirochætes with normal serum, or with serum of individuals convalescent from relapsing fever, Gabritschewsky showed that the latter acts specifically *in vitro* on the spirochæte. Sawtschenko and Melkich, whose results confirm those of Gabritschewsky, find that the spirillicidal bodies are destroyed at a temperature of 64° C., this probably bringing them into line with Ehrlich's amboceptors.

Relation of spirillicidal substances to the leucocytes.—Observations on the blood in cases of relapsing fever show that during the pyrexial paroxysm there is a progressive polymorphonuclear leucocytosis which reaches its acme before the crisis, the number of leucocytes thereafter rapidly diminishing. On measuring the spirillicidal curve at the same time, Melkich found that during the paroxysm the spirillicidal content of the serum is low, and that as the leucocytosis diminishes there is a "critical" development of the spirillicidal substances, which by some are held to have a leucocytic origin. The serum may also contain agglutinins, but these have no relation to the spirillicidal substances.

Sero-diagnosis and sero-prognosis during apyrexia.—The recognition of these spirillicidal substances in the blood during apyrexia has been utilised as an aid to the diagnosis of relapsing fever. The ability of the serum tested to inhibit the movements of the spirochæte in $\frac{1}{2}$-$1\frac{1}{2}$ hours at 37° C. is looked upon as a positive reaction, and as specific of relapsing fever (Loewenthal, Routkewitch). A negative result has one of two causes—(1) either the patient is just about to relapse, and the spirillicidal content of the serum is too small to be observed, or (2) the case is not one of relapsing fever. Loewenthal has also formulated certain prognostic rules from a study of the rapidity with which the spirochæte is immobilised in serum taken during apyrexia.

Natural immunity to Spirochæta Obermeieri.—We have already seen that with the exception of certain catarrhine monkeys, all other animals, which have hitherto been tested in this respect, enjoy a remarkable immunity from the pathogenetic effects of S. Obermeieri. The cause of the resistance is, however, unknown.

Immunity acquired by passing through an attack of relapsing fever.—The study of epidemics of relapsing fever down to the most recent times shows that the disposition in the case of man is almost universal. It is also certain that one attack of relapsing fever does not confer any lasting degree of immunity from subsequent attacks (Murchison, Welsh, Litten, Jenner, Christison, Carter). The monkey resembles man in susceptibility, although the disease is as a rule less severe, and experiments are not wanting to show that after one inoculation, which has yielded a positive result, a second inoculation may prove fruitless. A certain degree of passive immunity may also be established by treating monkeys

with large quantities of serum of other animals in which an active immunity has been established (Gabritschewsky). In any case, however, the degree of immunity is not high; neither is it very durable.

Systematic position of the relapsing fever parasite, and the occurrence of other spirilloses.—Although until recently Spirochæta Obermeieri has been classed among the fission-fungi, considerable doubts have been expressed on the correctness of this belief. The remarkable clinical course of the disease, the exclusive occurrence of the parasite in the blood, the failure to cultivate it outside the body, and the experiments by Tictin on its transference by bugs has raised the suspicion that it is more closely allied to the Protozoa than to the Schizomycetes. In other words, that it is an animal parasite. This has been rendered practically a certainty by Schaudinn in the case of Spirochæta Ziemanni in *Athene noctua*. This parasite is carried by *Culex pipiens*, and at first appears in the form of a trypanosome which ultimately becomes spirally twisted, so as to constitute what has hitherto been called a spirochæte. According to this view the spirochæte is simply a stage in the life-history of a trypanosome. Researches in the last few years have also shown that spirillar fever is not peculiar to man. A number of rapidly fatal spirochætal infections (spirilloses) have been demonstrated, especially in the case of birds. Thus Saccharoff (1890) discovered in Tiflis a very fatal infectious disease of geese caused by Spirochæta anserina. In 1903 Marchoux and Salimbeni found the S. gallinarum to be the cause of a violent epidemic in fowls in and near Rio Janeiro. In analogy with relapsing fever in man, they showed that the spirochæte is conveyed by a tick (*Argas miniatus*) in the body of which it can live for several months. Theiler has also described a spirillosis in cattle in the Transvaal, and most recently Drs. Dutton and Todd (1905) have described a human tick fever caused by spirilla which are conveyed by Ornithodorus. With the continued study of these spirilloses, it is not unlikely that much new light will be thrown on the intimate pathology and biology of the Spirochæta Obermeieri.

Schaudinn has recently demonstrated the presence of an extraordinarily fine spirochæte in the surface and in the depths of primary and secondary syphilitic lesions. By prolonged staining with Giemsa's modification of Romanowsky's stain the micro-organism (*Spirochæta pallida*) can be seen as a fine, spirally-wound thread, measuring 4-14 μ in length, and at most ·25 μ in width. This observation has received abundant confirmation from all sides, and Levaditi has demonstrated the micro-organism in congenital syphilis. That it is the actual cause of syphilis is rendered highly probable by its discovery by Metchnikoff in the lesions of experimental syphilis in the monkey.

WILLIAM BULLOCH.

Morbid Anatomy.—In Berlin in 1872-73 no fewer than 100 fatal cases occurred in the Charité Hospital alone; and there were therefore numerous opportunities of making careful inquiry into the morbid anatomy. The organs in which the most marked changes were found

were the spleen, blood, liver, heart, kidneys, bones, and muscles. The most important changes of all, both as regards structure and gravity of import to life, were those found in the spleen and heart.

An alteration was commonly observed in the muscular tissue of *the heart*, so grave as frequently to account for the fatal issue. The organ was flabby, the muscular tissue throughout pale, of a dirty grey-yellow colour, and friable. The muscular fibres were in many cases found to be fatty. The fatty and general degeneration found in the heart in relapsing fever equalled that seen in the most malignant septicæmic and puerperal fevers, and in diphtheria.

The spleen was very much enlarged, and at the same time softened. In different observations it is described as weighing in one case as much as 4½ lbs. avoirdupois, in another over 2 lbs. (920 grammes), in another about 1½ lb. (670 grammes), in another 15 oz., and again about ¾ lb. (330 grammes). There were two sets of changes—a diffuse general enlargement, usually accompanied with noticeable softening, on the one hand; and on the other the appearance of small yellow softened patches which in some cases reached the size of a horse-bean. Some observers have believed these patches to be due to infarctions. The enlargement took place in all directions, the capsule being tightly stretched and shiny, the tissue-substance softer than usual, though not exactly diffluent; the spleen-pulp dark blue-red, standing out strongly; the follicles considerably enlarged and often obliterated; their colour for the most part grey, though sometimes pure white or yellowish. The swelling of the spleen-pulp was mainly due to marked congestion of the vessels, and an abundant increase of the cell-elements.

As regards the morbid anatomy of the *liver*, some difficulty occurred in distinguishing the recent effects caused by relapsing fever from those frequently pre-existing effects caused by alcoholism. But, so far as could be made out, the increase in the size of the liver was greater than has been observed in any other of the infectious diseases. In one case the liver weighed 3620 grammes—almost 8 lbs. avoirdupois—an enormous increase. The organ was enlarged throughout, the lobules being also increased in size, so that their boundaries were rendered obscure; the cut surfaces were cloudy, and of a striking uniform grey-red colour. On microscopic examination there was cloudy swelling of the hepatic cells with fatty infiltration, and small-cell infiltration along the portal vein. Jaundice did not seem to bear any relation to the gravity of the cases, being well marked in some slight cases. On the other hand, out of sixty-five fatal cases only sixteen showed the presence of this symptom.

The *kidneys*, like the liver, were also much increased in size, sometimes weighing even twice their normal weight. The parenchyma was found soft and flabby, the cortical substance increased and showing cloudy swelling, the vessels and the Malpighian bodies for the most part pale. In other cases the cloudy swelling chiefly affected the straight tubules. There were found, besides, more or less abundant dark red spots,

specially numerous near the surface; and, converging thence in a radiating manner towards the papillæ, they could be traced, as red or brown spots or stripes, deeply into the tissue of the pyramidal substance. On microscopic examination it was found that not only were the tubuli more or less fatty, but also that the lumen of the urinary tubuli was filled partly with transparent fibrinous material, and partly with hæmorrhagic clots in the most diverse stages of coloration. For the most part these were met with in the lower parts of the convoluted tubes and of the loops of Henle; but hæmorrhages were often found also between the capsule of Bowman and the glomerular tufts. In addition, there was an abundant infiltration of small cells in the interstitial tissue.

The *lungs* showed hepatisation, and in some cases bronchiectasis and bronchitis.

The change in the *bones* caused by relapsing fever was mainly a reddening of the marrow. In some cases the diaphyses and epiphyses of the thigh-bones or humeri showed yellowish-white infarcts of irregular spotty character, varying in size from that of a hemp-seed to that of linseed. Sometimes they were discrete, sometimes united by thin bridges to coarser infiltrations.

Symptoms.—*The invasion* of relapsing fever is generally sudden, with rigors, headache, backache, and loss of strength; though the muscular weakness does not hinder patients from walking long distances to hospital, especially during the first day or two of the disease. In Bradford they would walk into the workhouse as late as the third or fourth day. I saw many cases, however, in which the symptoms appeared to set in gradually rather than suddenly. On the other hand, cases did occur very suddenly, but, so far as my recollection goes, comparatively rarely. More commonly the patient had been ailing for some time before giving in to the attack, and would present himself with a white, moist tongue, and complaining of general malaise, rheumatic pains in the limbs and joints, and headache. The invasion was not so gradual as to make it difficult to date the commencement, but it was rarely so sudden as Murchison described it to be—by no means so sudden as the onset of typhus or pneumonia. Still, on the whole, the writers who have recounted the symptoms seen in the various epidemics which have appeared in this country, especially those of 1819, 1826, 1828, and in the great epidemic of 1843, unite in the statement that the onset of the disease was sudden.

The period of incubation has varied in different epidemics. Sometimes the disease has broken out immediately after exposure to contagion; sometimes not till as many as fourteen days had elapsed. In Silesia in 1857 it was said to be longer—from a fortnight to three weeks (*vide* p. 1175).

But whether the attack come on suddenly, or be preceded by a period of anorexia or malaise, it is generally ushered in by rigors which may be slight or more severe, though they are generally severe. After being

put to bed the patients complain of headache, generally referred to the occiput and vertex, and not, as a rule, accompanied by delirium. Pains are also complained of in the back and limbs. The skin is hot and burning, and the patient is restless with a flushed face, although the rest of the skin generally shows a characteristically yellow hue. The temperature, during the first few days of the attack, is high, ranging from 102° to 105° F. or even higher. The pulse also is quick, and is said sometimes to reach even 140 on the second day. In my cases it usually rose at that period to 110-120, and it appeared to me to be higher during the relapse—when it might rise to 130, or 140, or even 160—than during the initial fever. These very high rates did not, however, seem to indicate any particular danger in the case. Death was very rare; but most of my patients were young adults, and they did not seem to have been much debilitated by hardship or starvation, and so were no doubt better fitted to struggle successfully with incidental illness. Although I did not observe any instance in which the pulse rose so high as 160 on the second or third day, I often saw a temperature of 104° F., and sometimes as high as 105°. Generally there was no rash, but in a considerable minority of my cases a rose-coloured rash was observed, not unlike the spots of typhoid fever, but individually smaller. This rash was never petechial. It appeared on the thorax, abdomen, and limbs. In one case a rash was seen twice during the attack; the spot was from one to two lines in diameter, was rose coloured, and scarcely distinguishable from that of typhoid fever. All these rashes disappeared in a day or two. The second appearance of the rash occurred just before the defervescence at the end of the relapse.

Some interest attaches to the question of *rash* in relapsing fever. Murchison, who met with it in 8 out of about 600 cases, says it consisted of small spots, or of a reddish mottling: sometimes it resembled measles, but more often it was undistinguishable from that of typhus at an early stage; yet it always disappeared under pressure, and faded after a few hours, or within three or four days at the latest. It came out sometimes during the first attack, sometimes in the relapse, and either as early as the third day or immediately before the crisis. Petechiæ were not uncommonly present. It is suggested by Murchison that the rash in some cases was urticarial. What I saw, and not in one case only, but in many, was neither petechial nor urticarial. In the epidemic of relapsing fever in Silesia in 1857 a rose-rash on the second or third day was the rule; and a considerable number of the cases seen in Bradford in 1869-70 showed the same feature, approximating, therefore, in character to those seen in Silesia rather than to those seen in other epidemics in this country.

The *respiration* is hurried, and varies from twenty-eight to forty a minute. A distressing cough is usually present, with rhonchus, sibilus, and harsh breathing on auscultation. I seldom saw expectoration, and in none of my cases did true pneumonia supervene; the signs indicated

rather congestion of the tracheo-bronchial mucous membrane than congestion or inflammation of the lung itself.

These symptoms continue for several days, five to seven as a rule, but in some cases I have known them persist for as many as nine, the patient complaining most of the nausea and sickness, and of pains in the limbs and joints. The skin remains persistently yellow, and in nearly all cases the area of hepatic dulness is increased, while that of the splenic is always so. In some of my cases the area of splenic dulness seemed to be actually continuous with that of the heart, the spleen appearing almost as large as another liver. Patients then complained of weight and tenderness at the part. Tenderness was also well marked over the liver in many cases, corresponding with the occurrence of *jaundice*, which was present in nearly every case. As the latter was so common, occurring in slight as well as in severe cases, I cannot agree with those observers who look on it as a formidable symptom; but it is possible that different epidemics have shown widely different characters in this as in other respects. The jaundice has no necessary connexion with head symptoms. According to Dr. Sandwith, jaundice was present in one out of every ten of his cases; but whereas the proportion among survivors is only 4 per cent, that among fatal cases is as high as 47 per cent. "There is no doubt," he says, "that this symptom is more frequent and more intense in severe than in mild cases, and I have never seen it during a relapse. When it occurs in prostrate patients with delirium and dry, brown, fissured tongue, it is extremely useful in diagnosing the disease from typhus."

The rest of the *digestive* system also shows signs of disturbance. Generally speaking the tongue remains moist, and covered with a yellowish-white fur. It is frequently red at the tip, and occasionally the whole organ may be brown and dry as in typhus. Frequent and persisting vomiting of greenish-yellow matter is often observed. This symptom is in some cases most distressing, and may persist during the whole of the primary fever, disappearing during the intermission and reappearing during the relapse. Thirst is also a common symptom. The bowels are constipated as a rule, but in some cases diarrhœa occurs, and in others the bowels act every other day or so. *Pregnant women* almost always abort, but often not till the relapse occurs.

After these symptoms have continued for five, seven, or nine days, the severity pursuing an increasing or climacteric course, and the patient complaining much of the nausea and sickness, and of the pains in the limbs and joints, a *crisis* suddenly occurs. A copious perspiration appears, or diarrhœa or epistaxis, or two or more of these phenomena concur, often ushered in by a rigor (during which I have known the thermometer to register a temperature as high as 105° F.), and immediately the patient feels quite well. The temperature may then fall through from 7° to 10° F., from 104° F. to 97° F., for instance, or even, as shown in the chart on p. 1185, from 104·5° to 92·5°, and the

pulse from 136 to 70 or so; and the patient who, a few hours before, was tossing helplessly in the height of the fever, perhaps even with paralysis of the sphincters and pharynx, suddenly declares himself quite well, and is with difficulty prevented from getting up. The rheumatic pains, vomiting, headache, and all the febrile symptoms having disappeared, he will profess great surprise if he is told that there is another period of illness in store for him. The crisis occurred almost always during the night.

Although I might succeed in keeping my patients in bed for a few days, yet they generally got up towards the close of the interval, and before the *relapse*, which often therefore came upon them with all the force of the onset of a new disease. As, however, by no kind of treatment did it appear possible to prevent the occurrence of the relapse, and as therefore no hope could be held out that rest in bed might save the patient from its onset, it appeared the less desirable to interfere with the patient's own inclinations. One of my patients, previously a soldier in India, had had repeated attacks of intermittent fever, and, being quite certain that the illness from which he was suffering in 1870 was of the same character as the attacks with which he had been so familiar in India, was quite incredulous when I told him he would have a relapse. This incident is quite in keeping with what has been observed in other epidemics, and reminds us of the classic case of Dr. Hughes Bennett, who had relapsing fever in the epidemic of 1843, when he was attended by Dr., afterwards Sir Robert Christison. When the patient was told by his medical attendant that "he was suffering from an attack of an old acquaintance" of Christison's, "whose face had not been seen for a good many years; that he had not yet done with it, and that he would have another attack, commencing with rigor, on the fourteenth day, Dr. Bennett expressed great astonishment." "Surprised," says Christison, "I will not say incredulous, Dr. Bennett replied that the relapse had no time to lose, as there were only two or three hours of the fourteenth day to run. It did, indeed, lose no time, for I must have scarcely reached home from his house before the rigor set in with violence."

The period of exemption from febrile symptoms—*the intermission*—is of variable duration. In my cases it usually seemed to last longer in those who defervesced early after the primary fever, and a shorter time when the primary fever had lasted longer. Thus the intermission extended to between nine and ten days in a case where the primary fever endured only six days; and only six days when the primary fever lasted between eight and nine. In the former case, therefore, the relapse took place on the fifteenth day, or between the fifteenth and sixteenth; in the latter between the fourteenth and fifteenth. But this rule is not invariable. The authorities state that the relapse generally occurs abruptly on the fourteenth day. It is ushered in by rigor. The duration of the relapse was from three to five days in the cases I saw. The usual duration appears to be three days. A relapse

occurred, so far as my observation extended, in every case without exception. The symptoms, similar to those of the primary fever, were often more severe; and one sometimes saw the tongue completely brown and dry as in typhus, and observed the pulse ranging at what, in other circumstances, would be considered the perilously high rate of 160. At the end of three or four days this set of symptoms usually came to a termination nearly, if not quite, as abrupt as that of the primary fever, the thermometer indicating a fall of 6° or 7° F., rarely of 10° F., and the pulse a corresponding diminution. The second crisis generally led to the establishment of complete convalescence, though sometimes a second relapse occurred. In such a case the symptoms were not so severe, nor the defervescence so sudden as before. In none of the cases which I saw did a third relapse occur.

It is worthy of remark that during convalescence, both during the intermission and after the relapse, the temperature and pulse both invariably sank considerably below the normal standard, and gradually rose as convalescence became more completely established until the normal was again reached. This sequence is observed no doubt in most of the acute diseases, but it seems to me that the temperature ranges lower after the elevation of the febrile stage of relapsing fever than in most other diseases. Thus a temperature of 96° F. was common at the commencement of the intermission; while in one of my cases, in which a second relapse occurred, the temperature during the second intermission was observed to be 94·5°, 95·6°, and 96° F. on successive days. Even lower temperatures may be registered.

Two *temperature* charts, Nos. 1 and 2, are reproduced here. The first is more or less typical of the records of temperature (and pulse) found in relapsing fever. These ranges may be defined as two or more sets of high readings in temperature, alternating with periods of complete apyrexia. I have, unfortunately, no observations on the temperature at the very beginning of the fever (though I have one observation of 103·5° F. on the second day), but the authorities state that it is very high, agreeing in this respect with the early stage of typhus, but differing from that of typhoid fever. In the two charts depicted, the temperature was 103·5° F. on the third day in one, and 104° and 105° on the fourth day in the other. The second chart shows the very great fall of temperature sometimes observed during the intermission.

The *pulse-rate* is also characteristic of the cases seen in the Bradford epidemic. The usual accounts, however, state the pulse-rate as higher than is shown in the chart. Thus 140 is said to be not uncommon, while 160 is said to be occasionally reached. An interesting point is, as I have said, that these rates do not seem to imply danger to the patient, much less do they prove the forerunners of a fatal termination. As with the temperature, so with the pulse, a sudden and extensive fall occurs at the end of the primary attack, and also at the termination

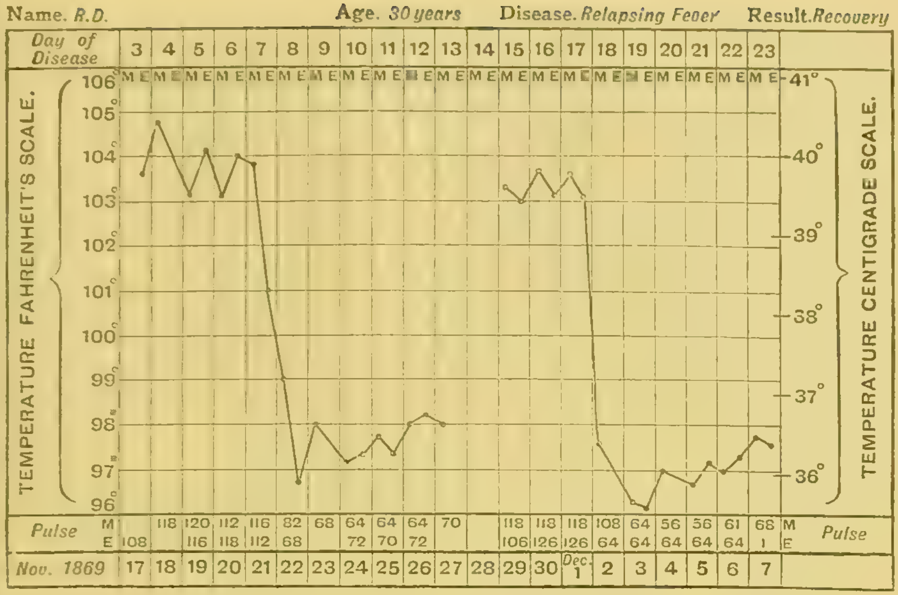

CHART 1.—Case of relapsing fever (Rabagliati).

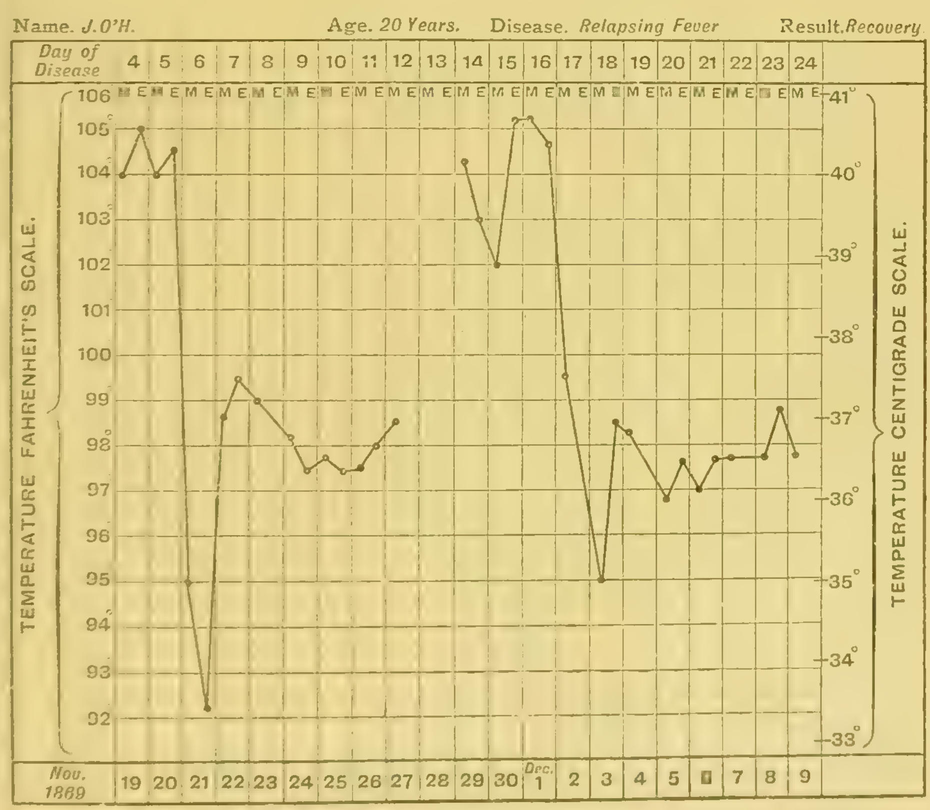

CHART 2.—Case of relapsing fever (Rabagliati).

of the relapse. One of my observations records a fall from 148 to 80, or of no fewer than 68 beats a minute in the course of a few hours. A fall from 120 to 60 in a night was quite a common occurrence. Like the temperature, the pulse also usually falls below normal before returning to its natural rate. Thus it remained for about a week at 60 a minute in a young fellow of eighteen, whose normal pulse-rate was much higher than that. The pulse and temperature, as might be anticipated, usually rise and fall together, though this is not always the case. Sometimes the rise of one precedes that of the other, and may be symptomatic of the general fever about to supervene. Both temperature and pulse gradually reach normal as convalescence becomes established.

The only fatal case which occurred in my practice was of an old woman of seventy. She died, like one of Hippocrates' cases, on the sixth day. As she did not live long enough to have the relapse, there was just that amount of doubt as to the diagnosis which must attach to every such case; but I had no doubt it was relapsing fever.

This course of the general symptomatology of relapsing fever is then very characteristic, and no one looking at these temperature charts could possibly mistake them, or confuse them with those of any other disease. No doubt anomalous cases occur. This is so in all epidemics, and not of relapsing fever only. In one case of mine the disease ran on for thirty-six days, and seemed to be a case in which typhoid and relapsing fevers were mixed together; although perhaps other explanations of it were possible. Yet the characters of the disease, as it was generally met with, were so striking and peculiar as to be readily separable from those of any other disease.

Relation between Relapsing and Typhus Fevers.—Some interest attaches to this subject. We have seen that Murchison thought that, in the matter of causation, there was some relation between these two diseases; he believed that relapsing fever was caused by destitution, while typhus fever was due to destitution and overcrowding. In the matter of the bacteriology of the two diseases no such relationship has been determined. At any rate as regards the progress of the two disorders in different epidemics a well-marked relation has been seen. The sequence has generally been that in epidemics of relapsing fever well-marked cases have been most numerous in the commencement of the epidemic, while cases of typhus were comparatively rare. As the epidemic advanced the cases of relapsing fever have become comparatively fewer, while those of typhus have become comparatively more numerous. Towards the close of the epidemic, on the other hand, the cases of typhus have become much the more numerous, while those of relapsing fever have been comparatively rare. Even as early as 1826 the distinction between the two fevers had been observed, but in 1843 it was more particularly insisted on, especially by Henderson. In Glasgow Infirmary, for instance, there were admitted 2871 cases of relapsing fever in 1843, and only 142 of typhus. In 1844, 432 cases

of relapsing fever were admitted, and 711 of typhus; while in 1845 only 37 cases of relapsing fever were received, and 266 cases of typhus, the mortality being, as might have been expected, much higher in the typhus than in the relapsing fever cases. In 1869-70 I saw a good many patients who first contracted relapsing fever, and in the course of a few weeks thereafter took typhus. I did not see any who took typhus first and had relapsing fever afterwards; and I doubt if there were any patients in Bradford in whom this sequence was observed. Such a sequence may, of course, have occurred in other epidemics.

In those cases in which typhus fever followed relapsing fever in the same patient within a short interval of time, it seemed to me that the typhus pursued a milder course. We might rather have anticipated that the patient, debilitated by the previous occurrence of relapsing fever, would thus have been brought into greater danger on the subsequent occurrence of typhus. Be this as it may, a relation between the numbers of cases of relapsing and typhus fevers has been observed as a rule in epidemics since the time when the two fevers were first distinguished. And before this time an investigation into the mortality at the beginning, middle, and end of epidemics has rendered it almost certain that a similar incidence of cases of relapsing fever and of typhus fever occurred.

During the continuance of the visitation of epidemic diseases in general, the mortality, as a rule, is highest at the onset of the epidemic, diminishing gradually as the epidemic advances. This may be because the most susceptible are first attacked, and take the disease in its most virulent form. "Increase of susceptibility" may be mistaken for "increased virulence" of disease, the former expression referring rather to the nature of the soil, so to speak, in which the disease finds a lodgment; while the latter refers rather to the nature of the seed than to the characters of the soil. Another reason for the diminishing mortality observed as epidemics advance in time may simply be that the disease assumes a milder form which we are unable to account for. In epidemics of relapsing fever, on the other hand, even before it was properly distinguished from typhus fever, we find records of a low mortality at the beginning of the epidemic, of an increasing mortality as the epidemic advanced, and of a mortality which was highest towards the close of the epidemic. This was particularly noticed in the epidemics of 1817-18 and in 1819; the most probable inference seems to be that there was a mixture of cases of relapsing and of typhus fever, and that their relative frequency at different periods of the epidemic determined the observed mortality. If that were so, as it appears to have been in 1817-19, as it certainly was in 1826-28, when the distinction between relapsing and typhus fevers was first made, and in 1843 and onwards, when it was generally accepted by the profession through the labours mainly of Henderson, it seems reasonable to suppose that, as a rule, relapsing fever and typhus fever have at other times borne to one another the relation which has been shown to exist in those epidemics.

Diagnosis.—The relationship just dealt with is to some extent helpful in the diagnosis of relapsing fever. As a rule, the severity of the onset is greater than in typhoid fever, and the absence of abdominal symptoms serves still further to distinguish it; although, of course, in some cases of typhoid, abdominal symptoms may be in abeyance, and on the other hand, in a few cases of typhoid the onset of symptoms may be both sudden and severe. As the cases progress the differences become more marked. Before the eruption of typhoid fever is due, a sudden defervescence will have revealed that the attack is one of relapsing fever. From typhus, again, the absence of rash in the majority of the cases of relapsing fever (though we have seen that in some cases a less characteristic rash has appeared both in this country and abroad) will serve to distinguish it. In both typhus and relapsing fever the onset may, of course, be sudden. But as between typhus and relapsing fevers the great and obvious difference is the sudden defervescence that characterises the latter at about the end of the first week; and this short convalescence will also serve to distinguish relapsing fever from pneumonia, in which the onset is likewise often sudden.

From small-pox the diagnosis is comparatively easy after the third or fourth day, the shotty eruption under the skin of the wrists and on the face in variola being never present in relapsing fever. In influenza—the epidemic which played such havoc with our people in 1890, and which has reappeared to greater or less extent every year since—the symptoms are as sudden as in relapsing fever; but they persist for a shorter time in mild cases, while in severe cases of influenza, bronchopneumonia almost always occurs. In influenza there is no sudden recovery and no subsequent relapse, the symptoms in influenza progressing pretty steadily to death or to some degree of convalescence.

All these points of difference which serve to distinguish relapsing fever from other diseases, such as typhoid and typhus fevers, small-pox, and pneumonia, are open to the objection that time is necessary for their appreciation. Is there no character, it may be asked, which will enable us at an earlier period to say positively—this is or is not relapsing fever? The demonstration of the parasite proper to the disease would do this; and Carter of Bombay found that no less than 25 per cent of his cases were irregular. The existence of the spirochæte of relapsing fever was unknown in 1869, so that I was not able to use it for diagnostic purposes. If, however, a new epidemic were to attack us, I think it would be found that the chief means of diagnosis would be time, as it has been in previous epidemics; especially as an observer might or might not think of relapsing fever if he had not had to treat it before. The discovery of the *spirochæte* would make the diagnosis sure.

Sequels.—These are not common in relapsing fever; with the termination of the attack itself the patient nearly always recovers, unless the illness occur in a very debilitated subject. In such persons as these the consequences, chiefly pulmonary, with which we are familiar in other fevers may follow relapsing fever. *Parotitis* must be especially

mentioned, not because of its frequency in Great Britain, where on the contrary it is very rare, but because in some epidemics—as in that which occurred in Russia about thirty-five years ago—its comparative frequency has led to the rumour of plague.

Prognosis is greatly determined by diagnosis. In relapsing fever we know that the mortality is not more than 5 per cent, while in typhus it may approach 20. The cautious physician will judge of each case on its merits, and after he has diagnosed relapsing fever, as he will no doubt be on the look-out for cases of typhus fever in the later phases of the epidemic, he will remember that a much higher mortality may then be looked for, although of course it will still remain true that relapsing fever has a low mortality. The higher mortality will probably be due to intercurrent typhus fever, and not to relapsing.

Treatment.—I think it may be taken as pretty certain that no drug essentially modifies the course of the disease. Relapsing fever, apparently, has its invasion, its primary five, seven, or nine days' fever, its intermission, and its relapse, in spite of all the resources of art. Some symptoms may be modified, but not apparently the great features of the disease. Thus several antiperiodics were used, without enabling me to prevent the occurrence of the relapse. The headache and arthritic pains were very severe, and though both were sometimes relieved by alkalis, it was often necessary to have recourse to opium. Colchicum seemed to have no effect on the pains. The persistent and distressing vomiting was very difficult of alleviation. Sometimes the effervescing draught, with or without hydrocyanic acid, was of service; sometimes relief was obtained by the administration of small and frequent doses of ipecacuanha, sometimes by sinapisms to the epigastrium; and in some cases all these resources were unavailing till the patient found relief in the natural issue of the disorder.

A. RABAGLIATI.

Serum-therapy in man.—Gabritschewsky immunised three horses with serum containing the spirochæte, the immune serum being afterwards utilised by Loewenthal on 131 cases of relapsing fever in man. The best results were obtained where the serum was injected on the third and fifth days of the first apyrexia, and in a considerable number of cases it appeared that the serum prevented the occurrence of the relapse: for whereas in cases untreated by serum only 25 per cent show no relapse, in the cases treated by Loewenthal over 40 per cent were arrested without a relapse. Still it cannot be claimed that the action of the serum in relieving the symptoms of the paroxysm is *éclatant*.

W. BULLOCH.

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